NON-INTERVENTIONAL (NI) FINAL STUDY REPORT

PASS information

Title	Post-Authorisation Safety Cohort Observation of Retacrit and Silapo (epoetin zeta) Administered Subcutaneously for the Treatment of Renal Anaemia (PASCO II)
Protocol number	Hospira (a Pfizer company): EPOE-09-11 (C1111006) STADA: PMS-830-09-0082
Version identifier of the final study report	3.0
Date	03 November 2020 Amended Report: 25 February 2021 and 23 March 2021
EU Post Authorization Study (PAS) register number	Retacrit: EUPAS4276 Silapo: not registered
Active substance	Epoetin zeta
Medicinal products	Retacrit Silapo
Product reference	Retacrit: MA number: EU/1/07/431/001-078 Silapo: MA number: EU/1/07/432/001-047
Procedure number	Retacrit: EMEA/H/C/000872 Silapo: EMEA/H/C/000760
Marketing Authorization Holders	Retacrit: Pfizer Europe MA EEIG Silapo: STADA Arzneimittel AG

Joint PASS	Yes
Research question and objectives	The primary objective of the observation was to estimate the incidence of Pure Red Cell Aplasia (PRCA), neutralising antibodies, lack of efficacy and thromboembolic events under treatment with Retacrit/Silapo (epoetin zeta) administered SC in patients with renal anaemia. The secondary objective was to obtain information on ADR associated with Retacrit/Silapo (epoetin zeta), use of epoetin zeta during pregnancy and lactation and data on long term use.
Countries of study	Bulgaria, Croatia, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Spain, Sweden, United Kingdom
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1. ABSTRACT (STAND-ALONE DOCUMENT)

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADA	antidrug antibodies
ADR	adverse drug reaction
AE	adverse event
AESI	adverse event of special interest
BAEU	BioAgilytix Europe GmbH
CHMP	Committee for Medicinal Products for Human Use
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
COVID-19	coronavirus disease 2019
CRA	clinical research associate
CRF	Case Report Form
CRO	Contract Research Organisation
CSR	clinical study report
EC	Ethics Committee
ECL	electrochemiluminescence
eCRF	electronic Case Report Form
EDC	electronic data capture
EEIG	European Economic Interest Grouping
EMA	European Medicines Agency
EPO	erythropoietin
ESA	erythropoiesis-stimulating agents
EU	European Union
GVP	Good Pharmacovigilance Practices

HLGT	higher level group term
ICD	Informed Consent Document
ICSR	Individual Case Safety Report
ID	identification
IEC	Independent Ethics Committee
IV	intravenous(ly)
LEC	Local Ethics Committee
MA	marketing authorisation
MAH	marketing authorisation holder
MedDRA	Medical Dictionary of Regulatory Activities
N/A	not applicable
NAb	neutralising antibody(ies)
NI	non-interventional
NIS	non-interventional study
PAC	post-approval commitment
PACL	Protocol Administrative Change Letter
PAS	Post-Authorisation Study
PASS	Post-Authorisation Safety Study
PASCO	Post-Authorisation Safety Cohort Observation
PRAC	Pharmacovigilance Risk Assessment Committee
PRCA	pure red cell aplasia
PT	preferred term
RIP	radio-immune-precipitation
SAE	serious adverse event

SAP	Statistical Analysis Plan
SAS	statistical analysis software
SC	subcutaneous(ly)
SD	standard deviation
SDV	source data verification
SmPC	Summary of Product Characteristics
SOC	system organ class
SOP	standard operating procedure
UK	United Kingdom

3. INVESTIGATORS

The names, affiliations, and contact information of the investigators at each study site are listed in Appendix 3.1.

This was a NIS; therefore, no principal or coordinating investigator was nominated.

4. OTHER RESPONSIBLE PARTIES

The Hospira (a Pfizer company) and STADA studies were conducted independently and the responsible parties for each study are summarised below. By mutual agreement a joint analysis of the combined data from the 2 studies was performed by Pfizer and is reported in this joint NIS report, prepared by MMS Holdings. Both Pfizer and STADA reviewed and approved the content of the NI final Study Report before finalization and submission to the EMA.

4.1. Hospira Study

Responsible Party Name and Affiliation	Role in the Study
Innovus Late Phase Division of Quality Metric Limited (Ingenix Inc) 12125 Technology Drive, Eden Prairie, Minnesota 55344, US	Study management (January 2010 – March 2012)
Monica Miess Innovus (Ingenix/i3) Senior Site Management Center Manager Late Phase Research Europe Max-Planck-Str. 4 85609 Dornach Germany	Study management (until March 2011)
Ana-Marija Malenica Innovus (Ingenix) (Deutchland) GmbH Wappenhalle Business Center Konrad-Zuse-Platz 8 81829 München Tel: +49 89 207042 603 Email: ana-marija.malenica@innovus.com	Study management (from March 2011)
Dr Liliana Smau-Frölich Advanced Medical Services (AMS) GmbH Am Exerzierplatz 2 D-68167 Mannheim, Germany	Investigator site monitoring and study management (excluding Greece and UK) (from March 2012)

Responsible Party Name and Affiliation	Role in the Study
Email: Liliana.Smau-Froelich@ams-europe.com **AMS GmbH sub-contractors:** Marijana Oremus Managing Director Synovia (March 2013 to June 2015) Boskoviceva 3/IV, 10000 Zagreb, Croatia Tel: +385 1 48 19 892 Marijana Oremus, Managing Director Oremus-Res (June 2015 to 31 May 2018) Tel: +385 1 28 53 199 Email: marijana.oremus@oremus-res.com Vladimir Goranov, CFO Comac Medical Ltd (from June 2018 onwards) South Side Business Centre, 38, Maystor Aleksi Rilets Str., 5th floor Res. Distr. Manastirski Livadi – West 1618 Sofia, Bulgaria Tel: +359 2 89 21 022 Email: vladimir.goranov@comac-medical.com Dr Dimitar Mirchev, Director CONVEX CRO 6, Tri Ushi str, 1000 Sofia, Bulgaria Tel: +359 2 98 63 109 Email: dimitar@convex.bg Philipp Rometsch, Project Manager mt-g medical translation GmbH & Co KG Stuttgarter Straße 155 D-89075 Ulm, Germany Tel: +49 731 176397 33	Investigator site monitoring and study management (Croatia) Investigator site monitoring and study management (Bulgaria) Translation services
Kalypso Kotsironi (site monitoring) Klairi Liakou (study management) Zeincro Hellas SA 30 Anapafseos str. 152 35 Vrilissia, Athens, Greece Tel: +30 210 8047709 Email: kliakou@zeincro.com	Investigator site monitoring and study management (Greece)

Responsible Party Name and Affiliation	Role in the Study
Zeincro sub-contractors: I.Varbobitis Address: 15 Sokratous str Kifissia Athens Greece Tel: +32 108 080113	Translation services
BAEU (formerly IPM Biotech GmbH) Lademannbogen 10 22339 Hamburg, Germany	Bioanalytical services
QPS LLC Delaware Technology Park 1 Innovation Way, Suite 200 Newark DE 19711 USA	Bioanalytical services[a]
DATATRAK International, Inc 6150 Parkland Blvd., Paragon II Bldg., Suite 100 Mayfield Heights Ohio 44124, USA	EDC system
Sandra L Drake, MPH, PhD Manager Corporate Quality Assurance MMS Holdings Inc. 6880 Commerce Blvd. Canton, MI 48187, USA Tel: +1 734 245-0157 (Ext. 157) Email: sdrake@mmsholdings.com	Medical writing (final study report and prose safety narratives)

a. In protocol amendment 4 for C1111006 the bioanalytical laboratory for Hospira ADA/NAb analysis was changed from Bioagylitix to QPS; however no further analyses were required before the end of the study so no ADA/NAb analyses were performed at QPS.

4.2. STADA Study

Responsible Party Name and Affiliation	Role in the Study
Dr Daniela Braun Advanced Medical Services (AMS) GmbH Am Exerzierplatz 2 D-68167 Mannheim, Germany Email: daniela.braun@ams-europe.com Tel: +49 62 17009 5162	Investigator site monitoring and study management; data management and statistics
BAEU (formerly IPM Biotech GmbH) Lademannbogen 10 22339 Hamburg, Germany	Bioanalytical services
QPS LLC Delaware Technology Park 1 Innovation Way, Suite 200 Newark DE 19711 USA	Bioanalytical services
Henning Lux Quadratek Data Solutions Novalisstr. 10 10115 Berlin, Germany Tel: +49 30 6883 64152 Email: HLux@clincase.com	Supplier of EDC system
Goutham Vasudev Clearight Information Systems, LLC 239 Main Street, E7, Pleasanton, California, USA Tel: +1 925 202 2330 Email: goutham.v@clearight.com	Coding Tool PACE

5. MILESTONES

Milestone	Planned Date	Actual Date	Comments
Date of IEC approval of C1111006 protocol. The IEC approval dates for the protocol and any amendments are provided in Appendix 3.2.	N/A	Date of first approval: 26 May 2010 Date of last approval: 13 Apr 2020	
Date of IEC approval of the PMS-830-09-0082 protocol. The IEC approval dates for the protocol and amendments are provided in Appendix 3.2.	N/A	Approval date for German Observational Plan V001: 27 Aug 2010 Notification date for German Observational Plan V004: 06 Dec 2019	Local EC submissions were the responsibility of the site.
Start of data collection for Retacrit	2010	07 Jul 2010	First patient first visit
End of data collection for Retacrit	27 Apr 2020	29 Apr 2020	Last patient last visit
Start of data collection for Silapo	N/A	28 Dec 2010	First patient first visit
End of data collection for Silapo	27 Apr 2020	29 May 2020	Last patient last visit
Registration in the EU PAS register: Hospira	Study started before EU PAS registration required	09 Jul 2013	
Registration in the EU PAS register: STADA	N/A	N/A	Not registered, as study started before EU PAS registration was required
Final report of study results	12 Oct 2020	03 Nov 2020	Report amended 25 Feb 2021 and 23 Mar

Milestone	Planned Date	Actual Date	Comments
			2021, Summary of Changes

6. RATIONALE AND BACKGROUND

Chronic renal failure is characterised by a progressive loss of kidney function resulting from disorders or conditions, such as diabetes mellitus or hypertension. In patients with chronic renal failure, deficiency of EPO production is the primary cause of anaemia.

EPO is an essential growth factor required for production of red blood cells. The stimulus for EPO production is believed to be the oxygen content of blood that is delivered to the renal interstitial cells. In individuals with correctly-functioning peritubular renal cells, low haemoglobin concentrations will result in increased quantities of EPO, resulting in increased red blood cell production (Ridley et al, 1994; Wang & Semenza, 1996; Lacombe & Mayeux, 1999).

Epoetin-associated PRCA is characterised by severe anaemia, low reticulocyte count, absence of erythroblasts, neutralising antibodies against EPO and as a consequence nonresponse to therapeutically administered epoetin. Between 1999 and 2004, a total of 191 patients with epoetin associated PRCA were identified across Australia, Canada, and certain countries in Europe and Asia. The majority of these cases (95%) were observed in haemodialysis patients who had received several months of treatment with epoetin alfa (Eprex) administered SC, using a particular formulation containing polysorbate 80 as stabilizer. Based on the increased rate of PRCA observed between 1999 and 2004, SC use was identified as a risk factor and patients with renal anaemia as an at-risk population. Exposure-adjusted incidence rates peaked in 2002 at 4.5 per 10,000 patient years (McKoy et al, 2008).

Changes in the formulation of the reference product (epoetin alfa), as well as subsequent pharmacovigilance efforts and safety guidance, resulted in a >95% decrease in the number of new cases of epoetin-associated PRCA. Since reformulation, antibody-mediated PRCA is regarded as a rare class-related toxicity that occurs after extended periods of SC administration of epoetins to chronic renal failure patients with an incidence rate of 0.02 to 0.03 per 10,000 patient years (McKoy et al, 2008).

This NIS (PASCO II) was designated as a PASS and was agreed by the CHMP in September 2012 in the context of the MA renewal (R/041). This PASS is part of the MAHs' commitment to the EMA, for further pharmacovigilance surveillance.

The joint PAC was to conduct a study with a prospective cohort of 6700 patients, each to be followed for 3 years of treatment with epoetin zeta. In order to fulfil this joint PAC to the EMA, Hospira, and STADA conducted separate observational studies with separate, but matching protocols and a total enrolment commitment of 6700 patients (4500 patients in the

Hospira study; 2200 patients in the STADA study). Following consultation with CHMP PRAC (PRAC rapporteur feedback received in May 2019), a protocol amendment was submitted to and approved by PRAC in November 2019 (EMEA/H/C/000872/MEA 033 and EMEA/H/C/000760/MEA 033) which reduced the overall sample size for the study to a minimum of 6206 patients (which was the joint enrolment total at the time of the consultation) in line with the observed incidence rate of PRCA. The observation of ongoing patients in the STADA study was planned to end on 27 Apr 2020, to coincide with the completion of 3-year follow-up for the last patient enrolled in the Hospira study. This enabled the Hospira and STADA data to be combined and reported to the EMA in a joint CSR by the end of 2020. Though the observation was planned to end on 27 Apr 2020, the last patient last visit for the STADA study was 29 May 2020.

The PASCO II joint data analysis presented in this report, represents data derived from 2 separate, but matching protocols: the Hospira study (C1111006) investigated treatment with Retacrit (MAH: Pfizer Europe MA EEIG); the STADA study (PMS-830-09-0082) investigated treatment with Silapo (MAH: STADA Arzneimittel AG). For the purposes of this PAC, STADA enrolled patients solely in Germany, whereas Hospira enrolled patients in a number of countries throughout Europe (including Germany).

Retacrit and Silapo are the trade names for the same product, epoetin zeta. The Drug Substance is manufactured by the same manufacturer in Germany, Norbitech GmbH. The Drug Product Retacrit is manufactured in Croatia by Hospira Zagreb d.o.o. and the Drug Product Silapo is manufactured in Germany by STADA Arzneimittel AG. When jointly referring to Retacrit and Silapo in this document, the name of the active product; epoetin zeta, will be used.

Following Pfizer's acquisition of Hospira in 2015 a Pfizer study ID C1111006 was also assigned. For the Hospira study, there are therefore 2 study IDs referenced in the report header and early sections of this report – the Pfizer study ID C1111006; and the Legacy Hospira ID EPOE-09-11. For simplicity, from this point forward the Pfizer study ID C1111006 will be used only.

Marketing authorization approval for Retacrit and Silapo (IV administration) throughout Europe was granted on 18 Dec 2007. In April 2010, the SC administration was approved in Europe (EMA opinion: 18 Feb 2010 and EC decision: 06 Apr 2010); procedure number for Retacrit: EMEA/H/C/000872/II/0020, procedure number for Silapo: EMEA/H/C/000760/II/0014.

Please note, "subject" and "patient" are used interchangeably in this CSR.

7. RESEARCH QUESTION AND OBJECTIVES

This observational study was performed to collect long-term safety data of patients with renal anaemia treated with epoetin zeta, and to detect cases of epoetin-associated PRCA to demonstrate that the incidence rate of PRCA with epoetin zeta treatment is substantially below the incidence of 4.5 per 10,000 patient years observed in 2002 (McKoy et al, 2008).

Primary objective:

- To estimate the incidence of PRCA, neutralising antibodies, lack of efficacy and thromboembolic events under treatment with Retacrit or Silapo administered SC in patients with renal anaemia.

Secondary objective:

- To obtain information on ADRs associated with Retacrit or Silapo, use of epoetin zeta during pregnancy and lactation and data on long term use.

8. AMENDMENTS AND UPDATES

8.1. Amendments to the Hospira Protocol

The global protocol for C1111006 (dated 30 Mar 2010) was amended 4 times. A high-level summary of changes for each amendment is presented in Table 1. The final protocol (Amendment 4, dated 02 Aug 2019) is provided in Appendix 2.

Additionally, a country-specific protocol amendment was created for Denmark, as sites in Denmark were not permitted to collect ADA samples for analysis of anti-EPO antibodies. All other elements of the Denmark-specific protocol matched the global study protocol. The final version of this protocol (Version 4.0, dated 28 Apr 2015) is provided in Appendix 2.

Table 1. Amendments to C1111006 Protocol

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment	Reason
4	02 Aug 2019	Substantial	Section 7.8.1	Change of bioanalytical laboratory and technical assay for ADA/NAb analysis. To document the reduction of planned sample size. To incorporate standard Pfizer safety reporting language from the current Pfizer NI study (NIS) protocol template.	Previous laboratory no longer supported the technical assay used for the study. To document the plan, following consultation with the PRAC, to reduce the planned total sample size for the study in line with the observed incidence rate of PRCA. Enrolment in the STADA study ended following this amendment, and observation of ongoing patients was changed to end in April 2020, when the last patient enrolled by Hospira was due to complete the 3-year observation. This was to permit the Hospira and STADA data to be combined and reported to the EMA in a joint CSR. The required combined sample size was updated from 6700 patients to 6206 patients, and the combined data is reported to the EMA in a joint CSR. Pfizer standard safety language was incorporated to ensure consistency with current Pfizer processes.
3	20 Mar 2015	Substantial	Abstract, Section 5, Section 6, Section 8, Section 9, Section 14	Addition of requirement to report occurrences of overdose and treatment error in order to comply with current guidance. Changes to sections relevant to safety reporting and guidance in order to be consistent with current guidance and practice. Removal of the Retacrit summary of product characteristics (SmPC) as an appendix in order to avoid unnecessary protocol amendments, if the SmPC was updated, in the future.	To remain consistent with current EMA GVP guidance and practices. To remove the SmPC as an appendix in order to avoid unnecessary protocol amendments, if the SmPC was updated, in the future.

Table 1. Amendments to C1111006

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment	Reason
3 (continued)	20 Mar 2015	Substantial	Abstract, Section 5, Section 6, Section 8, Section 9, Section 14	Clarification of wording of selection criteria regarding expected availability of patients for observation for 3 years.	To provide clarity regarding the eligibility criteria.
2	05 Mar 2012	Substantial	Section 8.8.1, Section 8.9.3	To provide clarification on the safety reporting form/s to be used for reporting AESIs.	AESIs to be documented on appropriate targeted AESI report forms.
1	05 Aug 2010	Substantial	Abstract, Section 8.5, Section 8.7	Removal of reference to specific SmPC version in protocol text.	To remove the need to update the protocol each time the SmPC was updated.

The final approved protocol also includes the following nonsubstantial/administrative changes which were previously documented in PACL:

- PACL dated 22 Nov 2016
    - Change to ADR/AESI reporting contact details and to ADR/AESI Report Forms following Pfizer acquisition of Hospira.
- PACL dated 16 May 2018
    - Extension of maximum observation period for PASCO II from 8 years to 12 years to reflect the extended period of study recruitment which was necessary to recruit the required number of patients for the study.
    - Change of name for IPM laboratories to BAEU.
    - Clarification of 'Legal Representative' definition for Informed Consent.
- PACL dated 21 Nov 2018
    - Transfer of MAH from Hospira UK Limited to Pfizer Europe MA European Interest Grouping (EEIG).
    - Abbreviation updates

These PACLs are provided for further information in Hospira Protocol v 5.0, Appendix 1.

8.2. Amendments to the STADA Protocol

The first approved version of the PMS-830-09-0082 protocol was English Version 002, dated 20 Feb 2010. This version of the protocol was the basis for German Version 001, dated 09 Mar 2010. English Version 002 was amended once, and German Version 001 was amended 3 times during the course of the study.

A high-level summary of amendments to the protocol is presented in Table 2. The final protocols (English Version 003, dated 16 Aug 2019 and German Version 004, dated 03 Dec 2019) are provided in Appendix 2.

Table 2. Amendments to PMS-830-09-0082 Protocol

Protocol version (Amendment number)	Date	Substantial or administrative amendment	Summary of amendment
Version 003 (English) (Amendment 1 [English]) Version 004 (German) (Amendment 3 [German])	16 Aug 2019 03 Dec 2019	Substantial	Reduction of sample size from 6700 patients to at least 6206 patients in line with the observed incidence rate of PRCA (1706 patients were planned to be recruited by STADA and the remainder will be from an identically designed trial with the same epoetin zeta, conducted by Hospira). Adaption of study duration: the observation of ongoing patients will end in April 2020, when the last patient enrolled by Hospira is due to complete the 3-year observation. Implementation of the intention of Hospira and STADA to submit a joint CSR.
Version 003 (German) (Amendment 2 [German])	15 Feb 2018	Substantial	Prolongation of recruiting time until end of 2019
Version 002 (German) (Amendment 1 [German])	11 Dec 2015	Substantial	Change of Sponsor from cell pharm AG to STADA Arzneimittel AG Change of contact details Changes in responsibilities between Sponsor and AMS Recruiting time added: 7 years Maximum study duration prolonged from 8 to 10 years

8.3. COVID-19 Considerations

The COVID-19 pandemic that emerged in early 2020 had a minimal impact on the Hospira and STADA studies.

In the Hospira study, the vast majority of patients had already completed/discontinued (and on-site monitoring and SDV had been performed) before February 2020, when COVID-19 cases started emerging in Europe. Restrictions on travel and local lock-downs from February 2020 prevented final on-site monitoring and SDV at a small number of sites prior to database release. However, the amount of data impacted by these limitations was very small and so this was determined to be low risk. Nineteen sites in 6 countries were affected; 1 site in Sweden, 2 sites in Bulgaria, 3 sites each in Spain and Greece, and 5 sites each in Croatia and Germany.

In the STADA study, the last on-site monitoring was performed in July 2019 as planned. Any further monitoring beyond this date was performed remotely. Restrictions on travel and local lock downs from February 2020 onwards did therefore not have any impact on the pre-defined SDV.

9. RESEARCH METHODS

Initially, the planned maximum duration of the observation for PASCO II study was a total of 8 years (including enrolment and a 3-year follow-up observation period for each individual patient) but this was extended to 12 years in May 2018 due to slow enrolment, in particular in the STADA study.

Refer to Section 7, Hospira Protocol v5.0 and Section 7, STADA protocol v3.0 in Appendix 2 for further detail on the research methods.

9.1. Study Design

PASCO II was an NI, longitudinal, multicentre, prospective cohort study of patients with renal anaemia treated with epoetin zeta SC. A minimum of 6206 patients were each to be followed for 3 years of treatment with epoetin zeta.

The decision to treat the patient with epoetin zeta was independent of the decision to enrol the patient in the study. All steps related to the selection, enrolment and treatment of patients were to be in accordance with standard medical care.

The study was primarily designed to verify that immunogenicity was not a concern from the SC use of epoetin zeta. Due to the large sample size, the study also provided useful information about the incidence of thromboembolic events in patients with renal anaemia treated with epoetin zeta.

Primary endpoints were to determine the incidence rates of AESIs (PRCA, neutralizing antibodies, lack of efficacy and thromboembolic events including cerebrovascular events [eg, cerebrovascular accident, cerebral infarction, cerebral haemorrhage, and transient ischaemic attack], deep vein thrombosis, myocardial infarction, and pulmonary embolism). Secondary

endpoints were incidence rates of ADRs and information on pregnancy/lactation exposure and long-term use.

9.2. Setting

This patient observation was conducted between July 2010 and May 2020 at nephrologists' practices and dialysis centres treating patients with renal disease in 12 European countries.

Patients were treated with epoetin zeta solution SC using the medically required individualised treatment dosage for each patient as determined by a patient's healthcare provider. The duration of epoetin zeta treatment was also at the discretion of the patient's healthcare provider, independent of their participation in this study. Administration and dosing of treatment was performed according to the current SmPCs for Retacrit and Silapo.

For each patient, it was planned that up to 3 years' observation would be documented. As described in Section 6, and as agreed with the PRAC, the observation of ongoing patients in the STADA study, was to end at the time the last patient in the Hospira study completed their 3-year follow-up. This meant that some patients in the STADA study discontinued prior to completing their 3-year follow-up (see Section 10.1.1).

The schedule of observations performed during the study is presented in Table 3.

Table 3. Schedule of Observation

Type of assessment planned	Entry examination Day 0	Ongoing	Final examination Week 156
Patient selection criteria	X	-	-
Informed consent	X	-	-
Pseudonymised patient identification	X	-	-
Demography	X	-	-
Exposure to ESA	X	-	-
Medical history	X	-	-
Retaining of blood samples for determination of neutralising antibodies	X[a]	X[b]	X[a]
Occurrence of pregnancy/lactation	X	X	X
ADR	-	X	X
AESI (primary endpoints)	-	X	X

a. If available.
b. If formation of antibodies is suspected or on request by the investigator.

Patients could discontinue their participation in the study at their own request without having to provide any reason. Decisions on treatment discontinuation or changes were solely based on medical reasons, independent of considerations of continuation in the observation. Patients who discontinued from epoetin zeta treatment because of AESIs, ADRs, or pregnancy were followed up until their medical condition resolved or stabilised. For patients

who prematurely discontinued participation in the observation, the reasons were documented in their CRF.

9.3. Patients

Patients who met the following criteria were eligible for enrolment in the PASCO II study:

- Patients who were started on treatment with Retacrit or Silapo administered SC for renal anaemia according to the current SmPC.
- Informed consent was given in writing after detailed information about the characteristics of this observation was provided by the investigator.
- Patients were available for at least 3 years of observation.

Patients were not eligible for enrolment if they had any contraindications per the current SmPC of Retacrit or Silapo.

9.4. Variables

AESIs (independent of causality) were primary endpoints, and ADRs (ie, all AEs for which a causal relationship with epoetin zeta is at least a reasonable possibility) were secondary endpoints. The occurrence of AESIs and ADRs was documented in the patient CRF, and detailed information was reported to the safety database. SAEs/AEs that did not fulfil the criteria of protocol-specified AESIs or ADRs were not expected to be captured in the patient CRF or safety database.

9.4.1. Primary Endpoints

Incidence rate of AESIs:

- Pure red cell aplasia;
- Neutralising antibodies;
- Lack of efficacy (as defined in the current SmPCs);
- Thromboembolic events including cerebrovascular events (eg, cerebrovascular accident, cerebral infarction, cerebral haemorrhage, transient ischaemic attack), deep vein thrombosis, myocardial infarction, and pulmonary embolism observed under treatment with Retacrit or Silapo administered SC in patients with renal anaemia.

Further details on information collected are provided in Section 7.8.1.1, Hospira Protocol v5.0 and Section 7.8.1.1, STADA protocol v3.0 in Appendix 2.

9.4.2. Secondary Endpoints

Descriptive evaluation including incidence rates of ADRs, exposure during pregnancy, lactation and long-term use.

The Hospira and STADA protocols differed slightly in their definition of ADRs. Both protocols quote the GVP Annex 1 definition of an ADR - "a causal relationship between a medicinal product and an AE is at least a reasonable possibility". The STADA protocol included causality assessments of "certain related", "probable related", "possible related", "unlikely related" and "not assessable" as a reasonable possibility of a causal relationship. This differed from the Pfizer approach, which is a conservative binary decision for drug causality (ie, related or not related) applied to decide whether there is "at least a reasonable possibility of a causal relationship between a suspected medicinal product and an adverse event" based on CIOMS III/V, ICH E2A, GVP VI R2 and EU ICSR Implementation Guide. STADA considered an event as an ADR if either the reporter's or the company's causality assessment fulfilled the definition of an ADR.

Further details on information collected are provided in Section 7.8.1.2, Hospira Protocol v5.0 and Section 7.8.1.2, STADA protocol v3.0 in Appendix 2.

9.4.3. Other Parameters

- Demographic data
- Medical history, including selected risk factors
- Other medical history (diagnosis leading to renal failure and dialysis information)
- Details on epoetin zeta treatment
- Premature termination

Further details on information collected are provided in Section 7.8.1.3, Hospira Protocol v5.0 and Section 7.8.1.3, STADA protocol v3.0 in Appendix 2.

9.5. Data Sources and Measurement

All steps related to the selection and enrolment of patients and the treatment of these patients were carried out in accordance with standard medical care. The decision to treat a patient with epoetin zeta was independent of the decision to enrol a patient in the study.

All participating investigators were asked about the availability of blood samples obtained from routine laboratory determinations before start of treatment with epoetin zeta (pre-dose serum sample)[1]. For patients who had pretreatment samples available (and who provided

[1] Not all countries/sites were permitted to participate in this aspect of the study based on their local regulations. For example, sites in Denmark were not permitted to participate.

their consent), samples were centrally stored and, if necessary, were analysed in a specialised laboratory for determination of neutralising antibodies. During the study, if suspected cases of PRCA occurred the option was available to investigators for blood samples to be analysed by a specialist central laboratory and this would include, if available, these routine pretreatment samples.

ADA Bioanalytical Methods

For suspected cases of PRCA, human serum ADA samples were analysed for the presence or absence of anti-EPO antibodies at BAEU (Hamburg, Germany), following a validated assay with a tiered approach using screening, confirmation and titre. The radioimmunoprecipitation assay was validated in compliance with BAEU Bioanalytical Method SOP and is documented in the method validation reports (BAEU Validation Report: IPM-2012-B-05-03, IPM-2014-B-05-06 and IPM-2016-B-01-10).

ADA in study assay performance was characterised by positive control (affinity purified anti-EPO rabbit polyclonal antibody) and negative control (human serum). The bioanalytical report corresponding to this work is included in Appendix 8.

NAb Bioanalytical Methods

The confirmed positive human serum ADA samples were further analysed for the presence or absence of neutralizing anti-EPO antibodies at BAEU (Hamburg, Germany). The cell-based NAb assay was validated in compliance with BAEU technical SOPs and is documented in the method validation reports (BAEU Validation Report: IPM-2014-B-05-07, IPM-2016-B-05-05 and IPM-17-060-065).

NAb Assay performance was characterised by positive control (rabbit anti-EPO polyclonal antibody sera) and negative control (human serum). The bioanalytical report corresponding to this work is included in Appendix 8.

The following patient information was collected:

- Pseudonymised patient identification
- Indication for treatment
- Previous treatment with epoetin zeta
- Informed consent
- Demographic data (including height and dry weight)
- Medical history including selected risk factors
- Exposure to ESAs

- Start of treatment with epoetin zeta
- Total weekly dosage of epoetin zeta
- Blood pressure and heart rate (as determined in normal clinical practice)
- First assessment of haemoglobin and haematocrit (as determined in normal clinical practice)
- ADRs
- AESIs and lack of efficacy
- Pregnancy and lactation periods, if applicable
- Concomitant medication

9.6. Bias

Blinding was not applicable in this non-comparative observational study. To minimize underreporting of ADRs and AESI, the investigator documented in the CRF at each patient visit, any AESIs/ADRs that had occurred in the period since the previous visit.

The decision to treat patients with epoetin zeta was independent of the decision to enrol patients into the study. According to GVP Module III B.3, subject to the healthcare professional's terms of service, payment was restricted to compensation of the healthcare professional for any additional time and expenses incurred. No additional payment or inducement for a healthcare professional to participate in this study was offered or given.

In order to avoid selection bias, physicians participating in this study were required to include patients who were started on treatment with epoetin zeta, and were willing to participate, consecutively.

9.7. Study Size

The observation had initially planned to enrol up to 6700 patients.

The study sample size was chosen to detect cases of epoetin-associated PRCA to demonstrate that the incidence rate under treatment with epoetin zeta is substantially below the incidence rate observed between 1999 and 2004, and that it can be reasonably concluded that the observed incidence is in the range of the incidence of the class of ESAs. The study was designed primarily to verify that no immunogenicity concern arises from the SC use of epoetin zeta. Due to the large sample size, this observation was also helpful in providing further information about the incidence of thromboembolic events in patients with renal anaemia treated with epoetin zeta.

In the STADA study, recruitment of patients was considerably lower than expected; thus, the planned number of patients was not enrolled within the anticipated timeframe. Following consultation with the PRAC in May 2019 and based on the observed PRCA incidence rate at that time, it was agreed that the planned total sample size for the study could be reduced to a minimum of 6206 (the total enrolment at the time of the consultation with the PRAC). It was further agreed that the follow-up of patients in the STADA study could be stopped at the end of April 2020, to coincide with completion of 3-year follow-up of the last patient in the Hospira study. This enabled the Hospira and STADA data to be combined and reported significantly earlier.

9.8. Data Transformation

AESIs and ADRs were recorded in the CRF and clinical database, however details of reported AESIs and ADRs, including onset and cessation dates, causality, seriousness, SAE criteria, action taken to study treatment and outcome included in this report were primarily obtained from the respective safety databases of the 2 study sponsors.

All other data, including demographic and baseline characteristics, medical history and study treatment were taken from the respective clinical databases.

Detailed methodology for data transformations are documented in the SAP, which is dated, filed and maintained by the sponsors (Appendix 4).

9.9. Statistical Methods

The SAP (Version 1, 27 Apr 2020) describes the statistical methods used for summarising and analysing the data collected in this study. The SAP is provided in Appendix 4.

The following analysis sets were used:

- **Enrolled set:** The enrolled set was defined as all patients who provided informed consent and were enrolled in the study. The enrolled set was used to summarize patient disposition, medical history and demographic and baseline characteristics.

- **Safety set:** The safety set was defined as all patients who received at least one dose of epoetin zeta during the observation period.

9.9.1. Main Summary Measures

The PASCO II study data set was derived from 2 matched observational, non-comparative studies sponsored by the 2 MAHs (Hospira and STADA) and any analyses carried out using the pooled data was descriptive and exploratory. Descriptive summary statistics were used.

9.9.2. Main Statistical Methods

The statistical analyses were performed using SAS Version 9.4.

9.9.2.1. Analyses for Continuous Data

Continuous variables are presented using descriptive summary statistics: number of observations, arithmetic mean, SD, median, minimum, and maximum values. The mean and median were displayed to one decimal place more than the raw value. The SD is displayed to 2 decimal places more than the raw value.

9.9.2.2. Analyses for Categorical Data

Categorical variables are presented using frequency counts and percentages. All percentages are reported to 1 decimal place.

9.9.2.3. Safety Analyses

All safety analyses were carried out using the safety set. The (crude) incidence rate was defined as the number of patients who experienced a certain event (eg, a specific MedDRA PT), divided by the number of patients who had been exposed to epoetin zeta (ie, epoetin zeta was administered at least once) after enrolment into PASCO II. The exposure-adjusted incidence rate was also evaluated using the number of patient years exposed to epoetin zeta as the denominator. In addition, cumulative AE incidences were derived from life table analysis for 2-monthly intervals. The cumulative incidence accounts for the actual duration of follow-up as well as the time pattern of when the events occurred relative to the number of patients in the safety set.

For the life table analysis, the time to onset of an event was defined as:

- 'observed' on the study day of first occurrence of the event for patients with the specific event, and
- 'censored' for patients without the specific event as the study day of patient's death (if applicable) or as the study day of the patient's discontinuation from the study.

In case an AE onset date was observed before the date of enrolment, the onset was assumed to have occurred on the date of enrolment for the life table analysis. Information on the calculation of study day is provided in Section 11.1 of the SAP in Appendix 4. The life table analysis was performed for all AESI/ADRs.

The 95% CIs for the incidence rates was calculated. If the number of AE on the MedDRA PT level was 0 or 1, the 95% CIs for crude rates was derived from the continuity-corrected "score interval method" (Vollset, 1993). CIs for the cumulative AE incidence was based on Greenwood's formula (Kalbfleisch & Prentice, 1980). It should be stated that the confidence limits were to be interpreted in an exploratory sense, not as exact statistical error probabilities.

9.9.2.4. Analysis of Treatment Exposure

Exposure to epoetin zeta for each patient was derived as the duration from the first dosing within PASCO II until study completion/termination date. Descriptive summary statistics for

treatment exposure was presented in days for all patients treated (safety set), and for a subset of pregnant and lactating women within the safety set.

In the Hospira study, for patients who were on Retacrit holiday (ie, had an interruption/break from their treatment with Retacrit) until the end of the study, treatment exposure was calculated as the duration from first dosing within PASCO II until the start of Retacrit holiday. For patients with interruptions between Retacrit treatments, interruptions more than 3 months were excluded from the calculation of total treatment exposure. However, in the STADA study, Silapo treatment holidays/interruptions were not reported.

9.9.3. Missing Values

Missing data were not imputed. AEs with partial/missing dates were imputed as follows:

- Partial onset date
    - For missing onset day, the first day of the month was used.
    - For missing onset month and day, the first day of the year was used.
    - If the imputed onset date fell in the same month as the date of first study treatment, then the onset date was reset to the date of first study treatment.
- Partial stop date
    - For missing stop day, the last day of the month was used.
    - For missing stop month and day, the last day of the year was used.
    - If the imputed stop date was earlier than the date of first study treatment, then the stop date was set to the date of first study treatment.
- Missing onset date
    - If first day of study treatment was earlier than AE stop date, then the onset date was set to first day of study treatment
- Missing stop date
    - The stop date was imputed as the latest of the patient withdrawal/completion date, death date, last day of treatment, or AE onset date

9.9.4. Sensitivity Analyses

The maximum observed epoetin zeta exposure for patients in the study was nearly 4 years (1 year longer than the maximum observation period specified in the protocol), because a number of patients in both studies had been withdrawn from the study later than the intended 3-year (ie, 36-month) observation period.

Since this was a real-world observational study where no visit schedule was required, a visit window of 2 months after the intended end of participation for each patient was considered appropriate (ie, 36 months + 2 months). In order to determine the impact on the study results of the longer observation periods in these patients a sensitivity analysis was performed, which excludes data collected >38 months after the date of informed consent.

Table 15.3.2a (Adverse Events), Table 15.3.4a (Exposure-Adjusted Incidence Rate of Adverse Events, AESI, and ADR other Than Events of Special Interest), Table 15.4.1.1a (Exposure to Epoetin Zeta) and Table 15.4.1.3a (Exposure to Epoetin Zeta in Patient-Years by Duration) were generated using the truncated data. In addition, a new table (Table 15.4.1.4) was generated to provide a summary with the number of patients observed for more than 38 months and the corresponding treatment exposure during the period of overrun.

9.9.5. Amendments to the Statistical Analysis Plan

A supplemental SAP was issued on 07 Sep 2020, to describe additional sensitivity analysis for the PASCO II CSR not included in the study SAP Version 1 (dated 27 Apr 2020). See Section 9.9.4 for high level description of sensitivity analyses.

9.10. Quality Control

The conduct of the study was supervised by designated monitors, who were trained in the indication. Scope, objective, responsibilities and procedures of monitoring were described in a monitoring manual. Checks for plausibility and completeness were performed automatically while entering data in the EDC system.

To avoid underreporting, quality assurance measures such as Investigator Training and Monitoring (Source Data Verification) were implemented.

Data handling was performed according to national data protection laws. Data were entered directly by the sites into the database (EDC) via electronic CRFs. An approval of the data by electronic signature was mandatory.

Source data checks were performed for:

- Confirmation of informed consent
- Documented AESI (primary endpoints)
- Documented ADRs

- Documented cases of pregnancy/lactation
- Confirmation that the patient is receiving SC epoetin zeta
- Documentation of serum samples and shipments (if applicable)

This study report has been subject to quality control review by the sponsors or the sponsors' designee.

9.11. Protection of Human Subjects

9.11.1. Patient Information and Consent

Written informed consent (Appendix 6) was to be obtained by study personnel, prior to the patient entering the study; the nature, purpose, and duration of the study was to be explained to each patient. Each patient was informed that he/she could withdraw from the study at any time and for any reason. Each patient was given sufficient time to consider the implications of the study before deciding whether to participate. Patients who chose to participate were to sign an informed consent document.

9.11.2. Independent Ethics Committee

The final protocol, any amendments, and informed consent documentation used by the sites were reviewed and approved by (or notified to) IEC(s) in accordance with local requirements.

9.11.3. Ethical Conduct of the Study

The study was conducted in accordance with the following legal and regulatory documents:

- Guideline on GVP Module VIII for PASS
- Directive 2001/83/EC, as amended, of the European Parliament and of the Council of 06 Nov 2001 on the Community code relating to medicinal products for human use
- Applicable national legislation
- SOP systems of the sponsors
- Applicable CRO SOPs.

10. RESULTS

10.1. Participants

10.1.1. Patient Disposition

A total of 6346 patients (4501 Retacrit, 1845 Silapo) were enrolled in this observational study of epoetin zeta in patients with renal anaemia. Of these, 6337 patients (4496 Retacrit, 1841 Silapo) received epoetin zeta and were included in the safety set.

Overall, 3763 (59.3%) patients discontinued from the study prior to completing the 3-year observation period. The most common reasons for discontinuation were:

- Patient death during the observation period: 1320 (20.8%) patients,
- Other reasons (not prespecified in the data capture system): 905 (14.3%) patients, and
- Patients being lost to follow-up: 873 (13.8%) patients.

Following implementation of STADA Protocol Amendment 1 (English Version 003 dated 16 Aug 2019), the observation of ongoing patients in the STADA study was planned to end on 27 Apr 2020, to coincide with the completion of 3-year follow-up for the last patient enrolled in the Hospira study. At that time, some patients in the STADA study had not completed a full 3-year observation period. The reason for discontinuation for these patients were reported as "Other". Though the observation was planned to end on 27 Apr 2020, the last patient last visit for the STADA study was 29 May 2020 (see Section 5).

A summary of patient disposition is presented in Table 4.

Table 4. Disposition Summary (Enrolled Set)

Number of Subjects	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
Disposition Phase: Enrollment			
Completed (Enrolled Set)	4501 (100.0)	1845 (100.0)	6346 (100.0)
Not Treated	5 (0.1)	4 (0.2)	9 (0.1)
Treated (Safety Set)	4496 (99.9)	1841 (99.8)	6337 (99.9)
Disposition Phase: Treatment			
Completed[a]	2014 (44.7)	560 (30.4)	2574 (40.6)
Discontinued from Study	2482 (55.1)	1281 (69.4)	3763 (59.3)
Subject Withdrew Consent	120 (2.7)	32 (1.7)	152 (2.4)
Subject No Longer Meets Inclusion/Exclusion Criteria[b]	473 (10.5)	134 (7.3)	607 (9.6)
Not in the Subject's Best Interest	59 (1.3)	0[c]	59 (0.9)
Occurrence of Adverse Event of Special Interest or Adverse Drug Reaction	25 (0.6)	86 (4.7)	111 (1.7)
Lack of Efficacy	8 (0.2)	0[c]	8 (0.1)

Table 4. Disposition Summary (Enrolled Set)

Number of Subjects	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
Lost to Follow-up	599 (13.3)	274 (14.9)	873 (13.8)
Death	888 (19.7)	432 (23.4)	1320 (20.8)
Other	335 (7.4)	570 (30.9)	905 (14.3)
Missing Reason for Discontinuation	0	23 (1.2)	23 (0.4)

a Subjects with a completed last study visit, a completed termination visit and the confirmation of regular study termination were considered as completed with the following exceptions:
Ten subjects in the Silapo group were documented by the study site as discontinued although they had completed the last study visit and had been observed for about 3 years. Since the termination visit was obviously incorrectly documented, these patients were considered as completed.
One subject in the Silapo group was observed for about 3 years and regular study completion was confirmed in termination visit. This subject was considered as completed despite missing the last study visit.
Two subjects in the Silapo group were documented by the study site as completed although they died before study end. Since the termination visit was obviously incorrectly documented, these patients were considered as discontinued.

b Subject No Longer Meets Inclusion/Exclusion Criteria included subjects who Switched to Another ESA Treatment.

c "Not in the subject's best interest" and "lack of efficacy" were not available as reasons for discontinuation in the STADA CRF.

Note: Subjects were counted once within each reason of discontinuation and may have had more than one reason to discontinue.
Source: Table 15.1.1

Listings of patients who discontinued the study and patients who were excluded from the analysis are provided in Appendix 7.1 and Appendix 7.3, respectively. Details of individual patient disposition is provided in Appendix 7.9.

10.1.2. Protocol Deviations

In the STADA study, no protocol deviations were recorded as due to the NIS design no deviations were defined in the study protocol.

In the Hospira study, major deviations were defined as those that were likely to affect the scientific value of the research plan or the rights, safety, or welfare of patients, and were assessed for any impact on the study conclusion.

At a minimum, protocol deviations related to the following (all of which are considered as major deviations) were documented:

- Breaches in the informed consent or data privacy processes
- Patient safety
- Statistical analysis

- Fraud

Major protocol deviations reported in the Hospira study are summarised in Table 5.

The majority of deviations related to the informed consent procedure.

Table 5. Major Protocol Deviations in Hospira Observation

Deviation Type	Deviation
Consent	Two patients (014, 019) at Site ES046 (Spain) signed the ICD with their fingerprint at their initial visit. At their next visit, an impartial witness for each patient formally signed the ICD on their behalf and confirmed they had received the study information and had provided their consent to participate in the study.
Inclusion/Exclusion Criteria	For 1 patient (001) at Site ES053 (Spain), 1 visit (6 months after study entry) was attended by the patient's daughter on behalf of the patient, as the patient was too ill to attend. Data entered for this visit were excluded from the data analysis.

Table 5. Major Protocol Deviations in Hospira Observation

Deviation Type	Deviation
Consent; Inclusion/Exclusion Criteria	For 1 patient (007) at Site ES053, all visits were attended by a relative of the patient on their behalf, and they also signed the ICD on behalf of the patient. The patient did not attend any visits in person. All data entered for this patient were excluded from the data analysis.
Consent	For 2 patients (023, 024) at Site FR064 (France) the original ICD (Version 1, dated 16 Apr 2010) was destroyed in error after the patients signed the updated version of the ICD (Version 5, dated 18 Jul 2013). The study CRA was not able to review the original ICDs. A comment was added to the updated ICD and signed by the investigator to confirm the initial consent by the patients. This action was verified by the study monitor.
Consent	For 1 patient (051) at Site GE012 (Germany), data were entered into the eCRF in error. No signed ICD was available for this patient, and the patient did not participate in the study. All patient data entered in error were deleted from the eCRF and excluded from the data analysis.

Table 5. Major Protocol Deviations in Hospira Observation

Consent	One patient (011) at Site GE454 (Germany) signed an ICD for minors because no ICD for adults was available at the site at the time. The patient later signed an adult ICD.
Consent	For 1 patient (009) at Site IT127 (Italy), data were entered into the eCRF, despite the patient not having signed the ICD. The patient did not participate in the study and the data entered in error was removed from the eCRF and was not included in the data analysis.
Consent	For 1 patient (017) at Site FR051 (France), the ICD was initially signed by a clinician who was not formally involved in the study. The ICD was resigned by the patient and principal investigator at a subsequent visit.
Inclusion/ Exclusion Criteria	One patient (002) at Site GE007 (Germany) did not fulfil the inclusion criteria for the study and was enrolled in April 2011 in error. The patient received treatment with IV Retacrit and not SC as required by the protocol. This was detected by the CRA in October 2012 and the patient was withdrawn from the study in November 2012 when they died. The patient was excluded from the safety set but included in the enrolled set.
Other	For 18 of 22 patients enrolled at Site GE067 (Germany) some source data were lost: • 14 x entry examination visits (13 of which included information about patient consent/entry into study) • 6 x visits 6 months after study entry • 1 x visit 12 months after study entry • 15 x study withdrawal visits Data that was not source verified prior to data loss were excluded from the data analysis. Data for 1 patient was not used at all, given that entry examination could not be verified.

Table 5. Major Protocol Deviations in Hospira Observation

Inclusion/Exclusion criteria	Two patients (073, 086) at Site GE093 (Germany) were incorrectly enrolled in the study. The patients received treatment with IV Retacrit and not SC as required by the protocol. The patients were withdrawn from the study, as they did not meet the inclusion criteria. Their data were included in the data analysis.
Consent	For 1 patient (001) at Site GE147 (Germany), a blood sample was sent to the central laboratory, following verbal consent by the patient, but prior to the patient having signed the ICD. The patient had already been withdrawn at the time this deviation was noted and the blood sample was not analysed.

10.2. Descriptive Data

10.2.1. Demographic and Baseline Characteristics

Demographic characteristics were comparable across both studies. A numerically higher proportion of male (55.5%) than female (44.5%) patients were included in the study. The majority of patients were Caucasian (98.2%), with a mean age of 71.2 years in Retacrit group (range: 0 to 99 years) and 70.7 years in the Silapo group (range: 18 to 97 years), a mean height of 167.6 cm and mean weight of 76.9 kg. Patients had mean haemoglobin values of 10.5118 g/dL (range: 5.957 to 18.998 g/dL), and mean haematocrit (proportion of 1.0) values of 0.3236 (range: 0.189 to 0.53) at baseline.

A summary of demographic and baseline characteristics, including vital signs is provided in Table 6. By-patient demographic and baseline data are provided in Appendix 7.4.

Table 6. Demographic and Baseline Characteristics (Enrolled Set)

	Statistic	Retacrit (N = 4501)	Silapo (N = 1845)	Total (N = 6346)
Age (Years)[a]				
	n	4500	1842	4500
	Mean (SD)	71.2 (13.81)	70.7 (14.0)	71.2 (13.81)
	Median	75.0	74.0	75.0
	Min, Max	0, 99	18, 97	0, 99
Sex				
Male	n (%)	2489 (55.3)	1034 (56.0)	3523 (55.5)
Female	n (%)	2012 (44.7)	809 (43.8)	2821 (44.5)
Missing	n (%)	0	2 (0.1)	2 (0.0)

Table 6. Demographic and Baseline Characteristics (Enrolled Set)

	Statistic	Retacrit (N = 4501)	Silapo (N = 1845)	Total (N = 6346)
Race[b]				
Asian	n (%)	16 (0.4)	8 (0.4)	24 (0.4)
Black	n (%)	6 (0.1)	4 (0.2)	10 (0.2)
Caucasian	n (%)	4408 (97.9)	1825 (98.9)	6233 (98.2)
Other	n (%)	4 (0.1)	6 (0.3)	10 (0.2)
Missing	n (%)	67 (1.5)	2 (0.1)	69 (1.1)
Height (cm)				
	n	4468	1843	6311
	Mean (SD)	166.9 (9.88)	169.2 (9.48)	167.6 (9.82)
	Median	167.0	169.0	168.0
	Min, Max	60, 202	120, 198	60, 202
Weight (kg)				
	n	4487	1843	6330
	Mean (SD)	75.66 (16.256)	79.83 (18.661)	76.87 (17.095)
	Median	74.00	77.50	75.00
	Min, Max	4.0, 179.5	31.0, 189.0	4.0, 189.0
Haemoglobin (g/dL)				
	n	4488	1841	6329
	Mean (SD)	10.4375 (1.36388)	10.6930 (1.36963)	10.5118 (1.37037)
	Median	10.4000	10.7000	10.5000
	Min, Max	6.100, 18.998	5.957, 16.900	5.957, 18.998
Hematocrit (Proportion of 1.0)				
	n	4446	1834	6280
	Mean (SD)	0.3220 (0.04213)	0.3274 (0.04131)	0.3236 (0.04196)
	Median	0.3200	0.3300	0.3200
	Min, Max	0.189, 0.509	0.19, 0.53	0.189, 0.53
Systolic Blood Pressure (mmHg)				
	n	4389	1816	6205
	Mean (SD)	135.6 (18.84)	133.7 (21.70)	135.0 (19.74)
	Median	135.0	131.0	135.0
	Min, Max	60, 228	60, 220	60, 228
Diastolic Blood Pressure (mmHg)				
	n	4387	1816	6203
	Mean (SD)	74.9 (11.52)	70.5 (13.00)	73.6 (12.14)
	Median	75.0	70.0	74.0
	Min, Max	30, 140	17, 120	17, 140
Heart Rate (bpm)[c]				
	n	4141	1568	5709
	Mean (SD)	73.1 (9.91)	71.4 (10.59)	72.6 (10.13)
	Median	72.0	71.0	72.0

Table 6. Demographic and Baseline Characteristics (Enrolled Set)

Statistic	Retacrit (N = 4501)	Silapo (N = 1845)	Total (N = 6346)
Min, Max	0, 142	0, 130	0, 142

a One enrolled patient in the Retacrit group has missing birth date information. Due to data protection reasons in Germany, age data for the STADA was transferred separately from other demographics data and was not included in the programmed summary table. Age data for Silapo included in the table was validated by Advanced Medical Services (AMS). Age data reported in the total column for Table 15.1.2, represent Retacrit data only (per programmed output).
b Subjects with Race = Other: European were counted as Caucasian.
c Heart Rate = 0 was documented for 1 subject in the Retacrit group and 1 subject in the Silapo group. For both subjects, it was confirmed that heart rate was not assessed.

Source: Table 15.1.2

10.2.2. Medical History

10.2.2.1. Risk Factors

The most frequent medical risk factors (≥20% of patients), assessed at baseline were:

- Hypertension: 5409 (85.23%) patients,
- Type 2 diabetes mellitus: 2564 (40.40%) patients,
- Hyperlipidaemia: 1955 (30.81%) patients, and
- Coronary artery disease: 1830 (28.84%) patients (Table 7).

By-patient data is provided in Appendix 7.4.1.

Table 7. Medical History: Selected Risk Factors Observed in ≥5% of Patients by Preferred Term in Either Group (Enrolled Set)

System Organ Class Preferred Term Type	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
Number of Subjects with at least one condition	4312	1814	6126
CARDIAC DISORDERS	1825 (40.55)	1040 (56.37)	2865 (45.15)
Atrial fibrillation	564 (12.53)	402 (21.79)	966 (15.22)
Cardiac failure chronic	716 (15.91)	531 (28.78)	1247 (19.65)
Coronary artery disease	1144 (25.42)	686 (37.18)	1830 (28.84)
Myocardial infarction	465 (10.33)	267 (14.47)	732 (11.53)
METABOLISM AND NUTRITION DISORDERS	2434 (54.08)	1229 (66.61)	3663 (57.72)
Hyperlipidaemia	1183 (26.28)	772 (41.84)	1955 (30.81)
Type 2 diabetes mellitus	1742 (38.70)	822 (44.55)	2564 (40.40)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	506 (11.24)	322 (17.45)	828 (13.05)
Neoplasm malignant	0	322 (17.45)	322 (5.07)
NERVOUS SYSTEM DISORDERS	453 (10.06)	298 (16.15)	751 (11.83)
Cerebrovascular accident	233 (5.18)	182 (9.86)	415 (6.54)
Cerebrovascular disorder	188 (4.18)	174 (9.43)	362 (5.70)
SOCIAL CIRCUMSTANCES	924 (20.53)	712 (38.59)	1636 (25.78)
Ex-tobacco user	624 (13.86)	522 (28.29)	1146 (18.06)
Tobacco user	300 (6.67)	190 (10.30)	490 (7.72)
VASCULAR DISORDERS	3828 (85.05)	1690 (91.60)	5518 (86.95)
Embolism venous	75 (1.67)	113 (6.12)	188 (2.96)
Hypertension	3752 (83.36)	1657 (89.81)	5409 (85.23)
Peripheral arterial occlusive disease	452 (10.04)	342 (18.54)	794 (12.51)

Source: Table 15.1.3.1

10.2.2.2. Diagnosis Leading to Renal Failure and Dialysis Information

Out of the 6343 patients with a diagnosis at baseline, the majority (4788 [75.45%]) were diagnosed with renal and urinary disorders, the most common of which were hypertensive nephropathy (1949 [30.71%]), diabetic nephropathy (1610 [25.37%]) and glomerulonephritis (696 [10.97%]).

Uncoded diagnoses were observed for 655 (35.50%) patients in the Silapo group (Table 8).

A full summary of all diagnoses leading to renal failure is presented in Table 15.1.3.2. By-patient data are provided in Appendix 7.4.2.

Table 8. Medical History: Diagnosis Leading to Renal Failure Observed in ≥10% of Patients by Preferred Term in Either Group (Enrolled Set)

System Organ Class Preferred Term	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
Number of Subjects with at least one condition	4500	1843	6343
RENAL AND URINARY DISORDERS	3600 (79.98)	1188 (64.39)	4788 (75.45)
Diabetic nephropathy	1167 (25.93)	443 (24.01)	1610 (25.37)
Glomerulonephritis	491 (10.91)	205 (11.11)	696 (10.97)
Hypertensive nephropathy	1409 (31.30)	540 (29.27)	1949 (30.71)
UNCODED	1 (0.02)[a]	655 (35.50)	656 (10.34)
Uncoded	0	655 (35.50)	655 (10.32)

a One patient in the Retacrit group had an event associated with the HLGT "Renal disorders (excl nephropathies)". The event should have been coded to the PT "Hypertensive nephropathy" under the SOC "Renal and Urinary Disorders", but was incorrectly programmed to Uncoded SOC.
Source: Table 15.1.3.2

Overall, 2274 (35.83%) patients (1236 [27.46%] Retacrit, 1038 [56.26%] Silapo) had a history of dialysis prior to study entry. The mean frequency of dialysis sessions per week was 3.1 (range: 0 to 7 sessions) (Table 9).

Table 9. Medical History: Dialysis Information (Enrolled Set)

System Organ Class Preferred Term	Statistic	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
Subject on Dialysis Prior to Study Entry?				
Yes	n (%)	1236 (27.46)	1038 (56.26)	2274 (35.83)
No	n (%)	3265 (72.54)	805 (43.63)	4070 (64.13)
Average Frequency of Dialysis per Week	n	1235	1033	2268
	Mean (SD)	3.1 (0.97)	3.0 (0.50)	3.1 (0.79)
	Median	3.0	3.0	3.0
	Min, Max	1, 7	0, 7	0, 7

Source: Table 15.1.3.3

10.2.2.3. Previous Treatment of Renal Anaemia

The most common prior ESA treatment was epoetin zeta. In the Retacrit group, 2216 (49.23%) patients had a prior history of receiving Retacrit and 14 (0.31%) patients had a

history of receiving epoetin zeta not specified as Retacrit, while 850 (46.07%) patients in the Silapo group had previously received epoetin zeta (Table 10).

A summary of all ESA treatments used in patients prior to study entry is presented in Table 15.1.3.4. By-patient data is provided in Appendix 7.4.3.

Table 10. Medical History: ESA Treatment Used by ≥2% of Patients by Preferred Term in Either Group (Enrolled Set)

ATC 3 Preferred Term	Retacrit (N = 4501) n (%)	Silapo (N = 1845) n (%)	Total (N = 6346) n (%)
OTHER ANTIANEMIC PREPARATIONS	2870 (63.76)	1075 (58.27)	3945 (62.17)
Aranesp	144 (3.20)	0	144 (2.27)
Darbepoetin Alfa	248 (5.51)	0	248 (3.91)
Epoetin Alfa	180 (4.00)	0	180 (2.84)
Epoetin Beta	207 (4.60)	0	207 (3.26)
Epoetin Zeta	14 (0.31)	850 (46.07)	864 (13.61)
Erythropoeitin Zeta	0	43 (2.33)	43 (0.68)
Methoxy Polyethylene Glycol-Epoetin Beta	120 (2.67)	0	120 (1.89)
Retacrit (Epoetin Zeta)	2216 (49.23)	0	2216 (34.92)
UNCODED	3 (0.07)	334 (18.10)	337 (5.31)
Epoetin Alpha	0	83 (4.50)	83 (1.31)
Epoetin Beta	0	38 (2.06)	38 (0.60)

Source: Table 15.1.3.4

10.3. Outcome Data

All patients included in the safety set (N = 6337) were evaluable for the primary safety endpoints.

10.4. Main Results – Safety Analysis

Note, AESIs and ADRs (other than AESIs) were the only clinical events required to be reported during this observational study. The use of "AE" in the following sections is used as a term to refer to the total number of AESIs and ADRs (other than AESIs) combined.
A high-level summary of AEs overall is presented in Table 11. Only protocol-specified AESIs and ADRs (other than AESIs) that were treatment-emergent in the study, are included in this CSR.

AESIs were reported for 418 (6.60%) patients and ADRs other than AESIs for 28 (0.44%) patients overall, details of which are provided in Section 10.4.1 and Section 10.4.2, respectively.

Table 11. Overall Summary of Adverse Events (Safety Set)

Subjects Evaluable for Adverse Events Number of Subjects	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Number of Adverse Events	252	316	568
Subjects Discontinued from Study Due to Adverse Events	125 (2.78)	119 (6.46)	244 (3.85)
Subjects Reporting Death Due to Adverse Events	70 (1.56)	73 (3.97)	143 (2.26)
Subjects with Adverse Events	199 (4.43)	242 (13.15)	441 (6.96)
Subjects with Serious Adverse Events	180 (4.00)	235 (12.76)	415 (6.55)
Subjects with Adverse Events of Special Interest	187 (4.16)	231 (12.55)	418 (6.60)
Subjects with Serious Adverse Events of Special Interest	178 (3.96)	231 (12.55)	409 (6.45)
Subjects with Adverse Drug Reactions other than Events of Special Interest	12 (0.27)	16 (0.87)	28 (0.44)
Subjects with Serious Adverse Drug Reactions other than Events of Special Interest	2 (0.04)	9 (0.49)	11 (0.17)

Adverse Events: total of AESI and ADR.
The table only includes protocol-specified AESIs or ADRs (other than AESIs) that were treatment-emergent in the study.
Five patients in the Silapo group had both AESIs and ADRs reported, therefore these 5 patients were counted twice.
Source: Table 15.3.2

Discontinuations due to AESIs or ADRs are summarized in Table 15.3.1. AEs and SAEs are summarized by SOC and PT in Tables 15.3.3.1 and 15.3.3.2, respectively. Fatal AEs are listed in Table 15.3.6. AEs are presented by patient in Appendix 7.7.

10.4.1. Adverse Events of Special Interest

The primary safety endpoint in this observational study was the incidence rate of AESIs, including PRCA, neutralising antibodies, lack of efficacy, and thromboembolic events, under treatment with epoetin zeta in patients with renal anaemia. AESIs are summarized in Table 12.

A total of 527 AESIs were reported for 418 (6.60%) patients overall. The most common AESIs were thromboembolic events, reported for 389 (6.14%) patients overall. PRCA was reported for 1 patient who also tested positive for neutralising antibodies (Appendix 7.7). Lack of efficacy was reported for 34 (0.54%) patients overall. Details of these events are provided in Section 10.4.1.1 through Section 10.4.1.4.

Table 12. Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Number of Subjects with at Least One Adverse Event of Special Interest	187 (4.16)	231 (12.55)	418 (6.60)
Number of Adverse Event of Special Interests	230	297	527
Pure Red Cell Aplasia	1 (0.02)	0	1 (0.02)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
Lack of Efficacy	12 (0.27)	22 (1.20)	34 (0.54)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	12 (0.27)	22 (1.20)	34 (0.54)
Drug ineffective	12 (0.27)	21 (1.14)	33 (0.52)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
Thromboembolic Events	176 (3.91)	213 (11.57)	389 (6.14)
CARDIAC DISORDERS	87 (1.94)	76 (4.13)	163 (2.57)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	0	4 (0.22)	4 (0.06)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	63 (1.40)	51 (2.77)	114 (1.80)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)

Table 12. Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	7 (0.16)	1 (0.05)	8 (0.13)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Transient ischaemic attack	8 (0.18)	10 (0.54)	18 (0.28)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	37 (0.82)	46 (2.50)	83 (1.31)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	12 (0.27)	0	12 (0.19)
Embolism arterial	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

Table 12. Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)

The table only includes protocol specified AESIs that were treatment emergent in the study.
Subjects were counted once within each system organ class or for each preferred term and may have had more than 1 AE.
MedDRA Version 23 coding dictionary was applied.
Source: Table 15.3.3.3

Out of the 527 AESIs reported (Table 12), 516 events in 409 (6.45%) patients were considered serious. A summary of serious AESI is provided in Table 13. Narratives for serious AESIs are included in Appendix 15.3.12.

Table 13. Serious Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Number of Subjects with at least one Serious Adverse Event of Special Interest	178 (3.96)	231 (12.55)	409 (6.45)
Number of Serious Adverse Event of Special Interests	219	297	516
Pure Red Cell Aplasia	1 (0.02)	0	1 (0.02)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
Lack of Efficacy	4 (0.09)	22 (1.20)	26 (0.41)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.09)	22 (1.20)	26 (0.41)
Drug ineffective	4 (0.09)	21 (1.14)	25 (0.39)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
Thromboembolic Events	174 (3.87)	213 (11.57)	387 (6.11)
CARDIAC DISORDERS	87 (1.94)	76 (4.13)	163 (2.57)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)

Table 13. Serious Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	0	4 (0.22)	4 (0.06)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	61 (1.36)	51 (2.77)	112 (1.77)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	6 (0.13)	1 (0.05)	7 (0.11)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Transient ischaemic attack	7 (0.16)	10 (0.54)	17 (0.27)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	36 (0.80)	46 (2.50)	82 (1.29)
Aortic thrombosis	0	1 (0.05)	1 (0.02)

Table 13. Serious Adverse Events of Special Interest by AESI, System Organ Class and Preferred Term (Safety Set)

Type of AESI System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	11 (0.24)	0	11 (0.17)
Embolism arterial	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified AESIs that were treatment-emergent in the study.
Subjects were counted once within each system organ class or for each preferred term and may have had more than 1 AE.
MedDRA v23 coding dictionary was applied.
Source: Table 15.3.3.4

10.4.1.1. Pure Red Cell Aplasia

One event of PRCA was reported for a patient in the Retacrit group on Study Day 250. Bioanalysis of a blood sample for the patient was positive for neutralising antibodies against EPO. The event was considered serious and related to epoetin zeta. The patient was withdrawn from the study due to this event, and due to lack of efficacy, reported as another separate serious AESI. The patient later recovered from the event of PRCA, while the event of lack of efficacy was unresolved (Table 13, Appendix 7.7). Details of these events are provided in the patient safety narrative in Appendix 15.3.12.

The incidence of PRCA derived from the life-table analysis with 2-monthly intervals was 0.000202 at 8 to 10 Months, and 0 through the rest of the observation period (Table 15.3.5.1).

In cases where lack of efficacy or Hb decreases (but no event of PRCA) were reported by the investigator, sites were contacted to provide the cause of the event in order to confirm or rule out that the reported events represent clinical signs or symptoms of potential immunogenicity or PRCA. For suspected PRCA cases, a confirmatory test for anti-EPO antibodies of a recent blood sample was offered.

10.4.1.2. Neutralising Antibodies

One patient in the Retacrit group with PRCA tested positive for neutralising antibodies against EPO as described in Section 10.4.1.1. Neutralising antibodies was not reported as an AESI for this patient.

The incidence of neutralising antibodies derived from the life-table analysis with 2-monthly intervals was 0.000213 at 10 to 12 Months, and 0 through the rest of the observation period (Table 15.3.5.2).

10.4.1.3. Lack of Efficacy

Lack of efficacy was characterised by an insufficient therapeutic response of the patient's haemoglobin levels to the administered dosage of epoetin zeta according to the judgement of the investigator.

Lack of efficacy was reported for 34 (0.54%) patients overall (Table 12), and was reported as serious in 26 (0.41%) patients overall (Table 13). Safety narratives for lack of efficacy events are presented in Appendix 15.3.12.

The following outcomes were reported for patients with lack of efficacy (though outcomes for some where unknown):

- Recovered: 10 patients, 8 of whom were switched to another ESA,
- Recovering: 1 patient who had been switched to another ESA,
- Not recovered: 12 patients, 3 of whom had been switched to another ESA, and
- Unknown: 11 patients (Appendix 7.7).

The incidence of lack of efficacy derived from the life-table analysis with 2-monthly intervals ranged from 0.00163 at the beginning of the study (0 to 2 months) to 0 at the end of the observation period (34 to 36 months). No obvious pattern in probability over time was observed (Table 15.3.5.3).

10.4.1.4. Thromboembolic Events

Overall, 389 (6.14%) patients reported at least one thromboembolic event during the study. Events were most commonly reported in the SOCs Cardiac Disorders (163 [2.57%] patients), Nervous System Disorders (114 [1.80%] patients) and Vascular Disorders (83 [1.31%] patients). The most frequent single event by PT was myocardial infarction, reported for 114 (1.80%) patients (Table 12).

The majority of patients for whom thromboembolic events were reported, had at least 1 serious event (387/389 patients). Serious events are summarized in Table 13. All events of myocardial infarction were considered serious. Details of these thromboembolic events are provided in the patient safety narratives in Appendix 15.3.12.

The incidence of thromboembolic events derived from the life-table analysis with 2-monthly intervals ranged from 0.00895 at the beginning of the study (0 to 2 months) to 0.00121 at the end of the observation period (34 to 36 months). No obvious pattern in probability over time was observed (Table 15.3.5.4).

10.4.2. Adverse Drug Reactions

The secondary safety endpoint in this observational study was the incidence rate of ADRs. ADRs were defined as all events where a causal relationship with epoetin zeta was at least reasonably possible. Only ADRs other than AESIs are reported here and are summarized in Table 14.

As described in Section 9.4.2, the Hospira and STADA protocols differed slightly in their definition of ADRs and it was decided for the safety analysis to follow the Hospira approach. For completeness, an additional table has been produced (Table 15.3.3.5a) to summarise events that would also have been defined as ADRs using the STADA approach. This additional table does not change the overall study results.

A total of 41 ADRs other than AESIs were reported for 28 (0.44%) patients overall. Five patients in the Silapo group had both AESI and ADR reported.

Five patients in the Silapo group had both AESI and ADR reported, therefore these 5 patients are counted twice (under AESI and ADR summary tables). Two cases in the Retacrit group that were reported in the clinical database as ADRs, did not meet the definition of ADRs, as both events were assessed clearly as unrelated to epoetin zeta by both the Investigator and the Sponsor. The CIOMS reports for these 2 cases are therefore not included in the CSR.

The most frequent single event by PT was haemoglobin decreased, reported for 5 patients overall (all in the Silapo group).

The majority of other ADRs were reported in 1 patient each. ADRs other than decreased haemoglobin reported in more than 1 patient each included:

- Malaise, headache, and pruritus (3 patients each), and
- Nausea, dizziness, and allergic dermatitis (2 patients each) (Table 14).

The incidence of ADRs derived from the life-table analysis with 2-monthly intervals ranged from 0.00277 at the beginning of the study (0 to 2 months) to 0 at the end of the observation period (34 to 36 months). No obvious pattern in probability over time was observed (Table 15.3.5.5).

Table 14. Adverse Drug Reactions Other Than Events of Special Interest by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Number of Subjects with at Least One ADR other than Events of Special Interest	12 (0.27)	16 (0.87)	28 (0.44)
Number of ADRs other than Events of Special Interest	22	19	41
CARDIAC DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Arrhythmia	0	1 (0.05)	1 (0.02)
Palpitations	1 (0.02)	0	1 (0.02)
GASTROINTESTINAL DISORDERS	3 (0.07)	1 (0.05)	4 (0.06)
Diarrhoea	1 (0.02)	0	1 (0.02)
Lip swelling	1 (0.02)	0	1 (0.02)
Nausea	1 (0.02)	1 (0.05)	2 (0.03)
Swollen tongue	1 (0.02)	0	1 (0.02)
Vomiting	0	1 (0.05)	1 (0.02)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.09)	0	4 (0.06)
Influenza like illness	1 (0.02)	0	1 (0.02)
Malaise	3 (0.07)	0	3 (0.05)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased[a]	0	5 (0.27)	5 (0.08)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	1 (0.05)	1 (0.02)
Bone pain	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	3 (0.07)	2 (0.11)	5 (0.08)
Dizziness	1 (0.02)	1 (0.05)	2 (0.03)
Dyskinesia	0	1 (0.05)	1 (0.02)
Headache	3 (0.07)	0	3 (0.05)
Somnolence	0	1 (0.05)	1 (0.02)
PSYCHIATRIC DISORDERS	1 (0.02)	0	1 (0.02)
Nightmare	1 (0.02)	0	1 (0.02)

Table 14. Adverse Drug Reactions Other Than Events of Special Interest by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (0.04)	0	2 (0.03)
Breast disorder	1 (0.02)	0	1 (0.02)
Vulvovaginal pruritus	1 (0.02)	0	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	4 (0.09)	5 (0.27)	9 (0.14)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis allergic	1 (0.02)	1 (0.05)	2 (0.03)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
Eczema	0	1 (0.05)	1 (0.02)
Hypertrichosis	0	1 (0.05)	1 (0.02)
Pruritus	2 (0.04)	1 (0.05)	3 (0.05)
Rash	1 (0.02)	0	1 (0.02)
VASCULAR DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Hypertension	1 (0.02)	0	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)

a These events were finally assessed as ADRs other than AESIs, as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
The table only includes ADRs (other than AESIs) that were treatment-emergent in the study.
Subjects are counted once within each system organ class or for each preferred term and may have had more than 1 AE.
Source: Table 15.3.3.5

Thirteen ADRs in 11 (0.17%) patients were considered serious. All events of decreased haemoglobin were considered serious. All other events were observed in 1 patient each, as shown in Table 15. Details of all ADRs are provided in the patient safety narratives in Appendix 15.3.12.

Two ADRs were fatal; 1 event of decreased haemoglobin and 1 event of gangrene, both in the Silapo group. Details of these events are provided in the patient narratives in Appendix 15.3.12.

Table 15. Serious Adverse Drug Reactions Other Than Events of Special Interest by System Organ Class and Preferred Term (Safety Set)

System Organ Class Preferred Term	Retacrit (N = 4496) n (%)	Silapo (N = 1841) n (%)	Total (N = 6337) n (%)
Number of Subjects with at Least One Serious ADR other than Events of Special Interest	2 (0.04)	9 (0.49)	11 (0.17)
Number of Serious ADRs other than Events of Special Interest	2	11	13
CARDIAC DISORDERS	0	1 (0.05)	1 (0.02)
Arrhythmia	0	1 (0.05)	1 (0.02)
GASTROINTESTINAL DISORDERS	1 (0.02)	0	1 (0.02)
Diarrhoea	1 (0.02)	0	1 (0.02)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased	0	5 (0.27)	5 (0.08)
NERVOUS SYSTEM DISORDERS	0	1 (0.05)	1 (0.02)
Dizziness	0	1 (0.05)	1 (0.02)
Somnolence	0	1 (0.05)	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
VASCULAR DISORDERS	0	1 (0.05)	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)

The table only includes ADRs (other than AESIs) that were treatment-emergent in the study.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
Two cases in the Retacrit group that were reported in the Clinical Database as ADRs, did not meet the definition of ADRs, as both events were assessed as unrelated to epoetin zeta by both the Investigator and the Sponsor. The CIOMS reports for these 2 cases are not included in the CSR.
MedDRA v23 coding dictionary was applied.
Source: Table 15.3.3.6

10.4.3. Exposure-adjusted Incidence Rate of AESI and ADRs Other Than Events of Special Interest

Crude and exposure-adjusted incidence rates, with the corresponding 95% CIs are presented in Table 16.

Only one patient had developed PRCA and was tested positive for neutralising antibodies during the study observation, which translates to 0.84 (95% CI: 0.04 – 5.49) per 10,000 patient-years.

There were 34 patients (0.29 [95% CI: 0.20 – 0.40] per 100 patient-years) who had lack of efficacy and 389 (3.37 [95% CI: 3.05 – 3.72] per 100 patient-years) who reported thromboembolic events.

There were 28 patients with ADRs other than events of special interest, which translates to 0.24 (95% CI: 0.157 – 0.342) per 100 patient-years.

Table 16. Exposure-Adjusted Incidence Rate of Adverse Events, AESI, and ADR Other Than Events of Special Interest (Safety Set)

	Number of Subjects with AE			Incidence Rate (Subjects with AE/100 Patient-Years)		
by AESI Term	Retacrit (N = 4496) n (%) [95% CI]	Silapo (N = 1841) n (%) [95% CI]	Total (N = 6337) n (%) [95% CI]	Retacrit Incidence per 100 patient-years [95% CI]	Silapo Incidence per 100 patient-years [95% CI]	Total Incidence per 100 patient-years [95% CI]
Adverse Events	199 (4.43) [3.8436, 5.0688]	242 (13.15) [11.6340, 14.7745]	441 (6.96) [6.3447, 7.6136]	2.3366 [2.0263, 2.6801]	8.1160 [7.1606, 9.1546]	3.8353 [3.4917, 4.2026]
Adverse Events of Special Interest	187 (4.16) [3.5945, 4.7845]	231 (12.55) [11.0678, 14.1477]	418 (6.60) [5.9972, 7.2354]	2.1949 [1.8943, 2.5287]	7.7244 [6.7925, 8.7399]	3.6315 [3.2972, 3.9895]
Pure Red Cell Aplasia	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0749]	0	0.0084 [0.0004, 0.0549]
Neutralising Antibodies	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0749]	0	0.0084 [0.0004, 0.0548]
Lack of Efficacy	12 (0.27) [0.1380, 0.4658]	22 (1.20) [0.7504, 1.8037]	34 (0.54) [0.3718, 0.7489]	0.1386 [0.0716, 0.2420]	0.6963 [0.4368, 1.0523]	0.2877 [0.1993, 0.4019]
Thromboembolic Events	176 (3.91) [3.3667, 4.5233]	213 (11.57) [10.1436, 13.1197]	389 (6.14) [5.5600, 6.7579]	2.0634 [1.7723, 2.3878]	7.0990 [6.2056, 8.0770]	3.3738 [3.0517, 3.7197]
ADRs other than Events of Special Interest	12 (0.27) [0.1380, 0.4658]	16 (0.87) [0.4976, 1.4075]	28 (0.44) [0.2938, 0.6380]	0.1385 [0.0716, 0.2418]	0.5061 [0.2896, 0.8206]	0.2368 [0.1574, 0.3420]

Adverse Events: total of AESIs and ADRs.
The table only includes protocol-specified AESIs or ADRs (other than AESIs) that were treatment-emergent in the study.
Confidence interval is displayed in percentages.
Two cases in the Retacrit group that were reported in the Clinical Database as ADRs did not meet the definition of ADRs, as both events were assessed as unrelated to epoetin zeta by both the Investigator and the Sponsor. The CIOMS reports for these 2 cases are not included in the CSR.
MedDRA v23 coding dictionary was applied.
Source: Table 15.3.4

10.5. Other Analyses

10.5.1. Exposure to Epoetin Zeta Including Long Term Use

The mean (SD) exposure to epoetin zeta was 666.4 (392.5) days (range: 1 day – 1437 days). The median exposure in the Retacrit group was 725.5 days, compared to 592.0 days in the Silapo group.

In both groups, the minimum exposure was 1 day, and in both groups, the maximum exposure exceeded the protocol-specified 3 years (±2 months) (Table 17). Treatment data at study entry are listed by patient in Appendix 7.5.

Table 17. Exposure to Epoetin Zeta (Safety Set)

	Statistic	Retacrit (N = 4496)	Silapo (N = 1841)	Total (N = 6337)
Exposure to Epoetin Zeta (in days)				
	n	4496	1841	6337
	Mean (SD)	681.7 (396.51)	629.0 (380.03)	666.4 (392.50)
	Median	725.5	592.0	687.0
	Min, Max	1, 1437	1, 1411	1, 1437

Source: Table 15.4.1.1

Overall, 84.0% of patients received treatment with epoetin zeta for up to 36 months in total, equating to 8703.0 patient-years (Table 18).

Sensitivity analysis excluding patients treated and observed beyond 38 months is presented and discussed in Section 10.5.3.

Table 18. Exposure to Epoetin Zeta in Patient-Years by Duration (Safety Set)

	Retacrit (N = 4496)		Silapo (N = 1841)		Total (N = 6337)	
Duration of Treatment	n (%)	Patient-Years	n (%)	Patient-Years	n (%)	Patient-Years
Cumulative up to 6 Months	715 (15.9)	186.7	276 (15.0)	66.5	991 (15.6)	253.3
Cumulative up to 12 Months	1296 (28.8)	679.4	563 (30.6)	275.6	1859 (29.3)	955.0
Cumulative up to 18 Months	1788 (39.8)	1354.4	856 (46.5)	639.3	2644 (41.7)	1993.7
Cumulative up to 24 Months	2261 (50.3)	2235.1	1081 (58.7)	1029.4	3342 (52.7)	3264.5
Cumulative up to 30 Months	2582 (57.4)	2991.1	1248 (67.8)	1403.0	3830 (60.4)	4394.1
Cumulative up to 36 Months	3766 (83.8)	6423.2	1556 (84.5)	2279.8	5322 (84.0)	8703.0
Cumulative up to and beyond 36 Months	4496 (100.0)	8667.2	1841 (100.0)	3170.3	6337 (100.0)	11837.6

Source: Table 15.4.1.3

10.5.2. Exposure to Epoetin Zeta During Pregnancy or Lactation

There were no reports of exposure to epoetin zeta during pregnancy or lactation during the observation period of this study (Table 15.4.1.2, Appendix 7.10).

10.5.3. Sensitivity Analyses

Overall, 144 patients (71 Retacrit, 73 Silapo) were treated and observed for longer than 38 months. The mean (SD) duration of exposure beyond 38 months was 50.2 (54.99) days (range: 1 day - 282 days) (Table 15.4.1.4).

Exposure for patients treated and observed up to 38 months, ie, excluding patients treated beyond 38 months is summarised in Tables 15.4.1.1a and 15.4.1.3a.

Two patients (in the Silapo group) had AESIs whilst receiving treatment beyond the 38-month period and were excluded from the AE summary table for sensitivity analyses (Tables 15.3.2 and 15.3.2a).

The impact on the exposure-adjusted incidence rate of primary and secondary endpoints is negligible (Tables 15.3.4 and 15.3.4a).

10.6. Adverse Events/Adverse Reactions

Refer to Section 10.4.1 and Section 10.4.2 for discussion of AESIs and ADRs other than AESIs, respectively.

Safety narratives for deaths, AESIs and ADRs, can be found in Appendix 15.3.12 for the Hospira study. Narratives for deaths and other serious and non-serious AEs entered in the STADA safety database are provided as an ICSR line listing in Appendix 15.3.12.

11. DISCUSSION

Between 1999 and 2004, a total of 191 patients with epoetin associated PRCA were identified across Australia, Canada, and certain countries in Europe and Asia. The majority of these cases (95%) were observed in haemodialysis patients who had received several months' treatment with epoetin alfa (Eprex) administered SC. Based on the increased rate of PRCA observed between 1999 and 2004, SC use was identified as a risk factor and patients with renal anaemia as an at-risk population. Exposure-adjusted incidence rates of PRCA for Eprex peaked in 2002 at 4.5 per 10,000 patient years.

This observational study was performed to collect long-term safety data of epoetin zeta in the treatment of patients with renal anaemia and to detect cases of epoetin-associated PRCA to demonstrate that the incidence rate with epoetin zeta treatment is substantially below the incidence rate observed for the reference product (Eprex) in 2002.

The primary endpoints were incidence rates of AESIs (PRCA, neutralizing antibodies, lack of efficacy and thromboembolic events). Secondary endpoints were incidence rates of ADRs and information on pregnancy/lactation exposure and long-term use.

The PASCO II joint data analysis presented in this report, represents data derived from 2 separate observational studies, with separate but matching protocols conducted by Hospira and STADA. Hospira (a Pfizer company) investigated treatment with Retacrit in a number of countries (including Germany) throughout Europe, while STADA investigated treatment with Silapo solely in Germany. The study was designated as a joint PASS and was part of a commitment of the MAHs (Hospira and STADA) to the EMA for further pharmacovigilance surveillance.

The patients were examined according to routine clinical care by investigators in their hospitals/practices at a baseline visit and under therapy (for planned 3 years' observation). Patients with diagnosed renal anaemia, who were started on treatment with epoetin zeta, were included in the observational study. Patients were treated with Retacrit or Silapo SC according to the approved SmPCs.

A total of 6346 patients (4501 Retacrit, 1845 Silapo) were enrolled in the study. Of these, 6337 patients (4496 Retacrit, 1841 Silapo) received study treatment and were included in the safety set. Overall, 3763 (59.3%) patients discontinued from the study prior to completing the observation period.

A slightly higher proportion of male (55.5%) than female (44.5%) patients were included in the study. The majority of patients were Caucasian (98.2%), with a mean age of 71.2 years in Retacrit group and 70.7 years in the Silapo group, mean height of 167.6 cm and mean weight of 76.9 kg.

11.1. Key Results

The overall incidence rates for predefined AESIs and ADRs were as follows:

- AESIs overall: 527 events in 418 (6.60%) patients.
    - PRCA: 1 (0.02%) patient (in the Retacrit group) (same patient tested positive for neutralising antibodies),
    - Lack of efficacy: 34 (0.54%) patients,
    - Thomboembolic events: 389 (6.14%) patients.
- ADRs: 41 events in 28 (0.44%) patients.

A higher proportion of patients in the Silapo group than in the Retacrit group had AESIs (12.55% vs 4.16%) and ADRs (other than AESIs) (0.87% vs 0.27%) during the study. AESIs of thromboembolic events were observed for 11.57% vs 3.91% of patients in the Silapo and Retacrit groups, respectively. This may be explained by the fact that a higher proportion of patients in the Silapo group were on dialysis prior to study entry (56.26% vs 27.46%), and had a medical history of selected risk factors, and were thus more likely to present with AEs. Of note, coronary artery disease was observed for 37.18% vs 25.42% of patients, Type 2

diabetes mellitus for 44.55% vs 38.70%, and hyperlipidaemia for 41.84% vs 26.28% of patients in the Silapo and Retacrit groups, respectively.

11.2. Limitations

The main limitation of a non-comparative observational study is the lack of a randomised control; this fact can create possible bias and can also mask cause-effect relationships or suggest false correlations.

11.2.1. Potential Statistical Limitations

The original planned sample size for the study was 6700 patients. Per consultation and agreement with the PRAC, the study sample size was reduced to a minimum of 6206 patients, as described in Section 9.7. This decrease in sample size translated to slightly wider CIs around the estimated incidence rates. However, even with the slight loss of precision in the CIs, the results still showed the exposure-adjusted incidence rate of PRCA (0.84 per 10,000 patient-years) to be significantly lower than the comparison rate (4.5 per 10,000 patients-years), and that rates of other AESIs are within the known safety profile of epoetin zeta.

Some patients were observed in the study for longer than the planned 3 years. This may have resulted in a greater number of safety events being reported for these patients, which could potentially have increased the estimates of incidence rates. However, as shown in discussion of sensitivity analysis Section 10.5.3, which excluded patients for whom data were collected longer than planned, the impact was negligible.

11.2.2. Other Potential Limitations

No predefined visit schedule was used in the study, but patients were generally encouraged to visit the study site at least once every 6 months. Due to the period of time between visits, there was the potential for patients to forget to report some safety events that had occurred since the last visit.

The study was conducted over a 10-year period so there were inevitable changes in investigators, site staff and sponsor study team members as well as closures of some study sites long before the completion of the entire study. While site monitoring and data review were done routinely throughout the study not all queries raised could be addressed by the end of the study.

A number of patients discontinued from the study before the intended 3-year observation period was complete. There were multiple reasons for patient withdrawal from the study, the most common specified reasons being death (20.8% patients overall) and patients who were lost to follow-up (potentially due to the long follow-up commitment required) (13.8% patients overall). Overall, 14.3% of patients discontinued due to reasons recorded as “Other”. As outlined in Section 10.1.1, some patients in the STADA study were discontinued prior to completion of 3-year observation period, following implementation of STADA

Protocol Amendment 1 (English Version 003 dated 16 Aug 2019), and coinciding with the completion of the 3-year observation period of the last patient in the Hospira study.

11.3. Interpretation

A single event of PCRA was observed in 1 patient out of 6337 patients included in the safety set for this observational study. The exposure-adjusted incident rate of PCRA was 0.84 per 10,000 patient years, which is substantially lower than the incidence rate of 4.5 per 10,000 patient years observed for Eprex in 2002.

The overall percentage of patients with other AESIs were low; lack of efficacy was observed for 0.54% of patients and thromboembolic events for 6.14% of patients. For thromboembolic events, the frequency category in the current EU SmPC is "Common" (>1/100 to <1/10, ie, >1% to <10%), which is consistent with observed frequency in PASCO II (6.14%).

11.4. Generalizability

Study data can be generalized because this NIS was conducted in a broad real-world study population in more than 10 European countries and with very few inclusion criteria.

12. OTHER INFORMATION

None.

13. CONCLUSIONS

With only 1 reported case of PRCA during the observation period, the incidence rate under treatment with epoetin zeta is substantially below the risk observed in 2002 for innovator's reference product (Eprex). Based on the observed incidence rate in this study, there is no immunogenicity concern over the SC use of the biosimilar product epoetin zeta in patients with renal anaemia. In addition, results for other AESIs and ADRs did not identify new safety concerns. No pregnant or lactating women were exposed to epoetin zeta during the study.

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15. LIST OF SOURCE TABLES AND FIGURES

Number of Subjects	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Disposition Phase: Enrollment			
Completed (Enrolled Set)	4501 (100.0)	1845 (100.0)	6346 (100.0)
Not Treated	5 (0.1)	4 (0.2)	9 (0.1)
Treated (Safety Set)	4496 (99.9)	1841 (99.8)	6337 (99.9)
Disposition Phase: Treatment			
Completed[a]	2014 (44.7)	560 (30.4)	2574 (40.6)
Discontinued from Study	2482 (55.1)	1281 (69.4)	3763 (59.3)
Subject Withdrew Consent	120 (2.7)	32 (1.7)	152 (2.4)
Subject No Longer Meets Inclusion/Exclusion Criteria[b]	473 (10.5)	134 (7.3)	607 (9.6)
Not in the Subject's Best Interest	59 (1.3)	0	59 (0.9)
Occurrence of Adverse Event of Special Interest or Adverse Drug Reaction	25 (0.6)	86 (4.7)	111 (1.7)
Lack of Efficacy	8 (0.2)	0	8 (0.1)
Lost to Follow-up	599 (13.3)	274 (14.9)	873 (13.8)
Death	888 (19.7)	432 (23.4)	1320 (20.8)
Other	335 (7.4)	570 (30.9)	905 (14.3)
Missing Reason for Discontinuation	0	23 (1.2)	23 (0.4)

[a] Subjects with a completed last study visit (follow-up 12), a completed termination visit and the confirmation of regular study termination are considered as completed with the following exceptions:
Subjects De-019-B031, De-019-B040, De-022-B015, De-063-B001, De-073-B003, De-078-B001, De-078-B004, De-078-B005, De-100-B006 and De-100-B017 in the Silapo group were documented by the study site as discontinued although they had completed follow-up visit 12 and had been observed for about 3 years. Since the termination visit was obviously incorrectly documented, these patients are considered as completed.
Subject De-054-B002 in the Silapo group was observed for about 3 years and regular study completion was confirmed in termination visit. This patient is considered as completed despite missing follow-up visit 12.
Subjects De-098-B068 and De-098-B095 in the Silapo group were documented by the study site as completed although they died before study end. Since the termination visit was obviously incorrectly documented, these patients are considered as discontinued.
[b] Subject No Longer Meets Inclusion/Exclusion Criteria includes subjects who Switched to Another ESA Treatment.
Note: Subjects are counted once within each reason of discontinuation and may have had more than one reason to discontinue.
PFIZER CONFIDENTIAL Source Data: Appendix 7.9 Date of Table Generation: 17AUG2020 (16:15)

	Statistic	Retacrit (N = 4501)	Silapo (N = 1845)	Total (N = 6346)
Age (Years)[a]				
	n	4500		4500
	Mean (SD)	71.2 (13.81)		71.2 (13.81)
	Median	75.0		75.0
	Min, Max	0, 99		0, 99
Sex				
Male	n (%)	2489 (55.3)	1034 (56.0)	3523 (55.5)
Female	n (%)	2012 (44.7)	809 (43.8)	2821 (44.5)
Missing	n (%)	0	2 (0.1)	2 (0.0)
Race[b]				
Asian	n (%)	16 (0.4)	8 (0.4)	24 (0.4)
Black	n (%)	6 (0.1)	4 (0.2)	10 (0.2)
Caucasian	n (%)	4408 (97.9)	1825 (98.9)	6233 (98.2)
Other	n (%)	4 (0.1)	6 (0.3)	10 (0.2)
Missing	n (%)	67 (1.5)	2 (0.1)	69 (1.1)
Height (cm)				
	n	4468	1843	6311
	Mean (SD)	166.9 (9.88)	169.2 (9.48)	167.6 (9.82)
	Median	167.0	169.0	168.0
	Min, Max	60, 202	120, 198	60, 202
Weight (kg)				
	n	4487	1843	6330
	Mean (SD)	75.66 (16.256)	79.83 (18.661)	76.87 (17.095)
	Median	74.00	77.50	75.00
	Min, Max	4.0, 179.5	31.0, 189.0	4.0, 189.0
Haemoglobin (g/dL)				
	n	4488	1841	6329
	Mean (SD)	10.4375 (1.36388)	10.6930 (1.36963)	10.5118 (1.37037)
	Median	10.4000	10.7000	10.5000
	Min, Max	6.100, 18.998	5.957, 16.900	5.957, 18.998
Hematocrit (Proportion of 1.0)				
	n	4446	1834	6280
	Mean (SD)	0.3220 (0.04213)	0.3274 (0.04131)	0.3236 (0.04196)
	Median	0.3200	0.3300	0.3200
	Min, Max	0.189, 0.509	0.19, 0.53	0.189, 0.53
Systolic Blood Pressure (mmHg)				
	n	4389	1816	6205
	Mean (SD)	135.6 (18.84)	133.7 (21.70)	135.0 (19.74)
	Median	135.0	131.0	135.0
	Min, Max	60, 228	60, 220	60, 228
Diastolic Blood Pressure (mmHg)				
	n	4387	1816	6203
	Mean (SD)	74.9 (11.52)	70.5 (13.00)	73.6 (12.14)

[a] One enrolled patient in the Retacrit group has missing birth date information. Age for treatment group SILAPO is not included in the data transfer.
[b] Subjects with RACE = Other: European are counted as Caucasian.
[c] Heart Rate = 0 was documented for 2 subjects: Uk-001-0001 in the Retacrit group and De-086-B021 in the Silpao group. For both subjects it was confirmed that heart rate was not assessed.
PFIZER CONFIDENTIAL Source Data: Appendix 7.4 Date of Table Generation: 22FEB2021 (17:21)

	Statistic	Retacrit (N = 4501)	Silapo (N = 1845)	Total (N = 6346)
	Median	75.0	70.0	74.0
	Min, Max	30, 140	17, 120	17, 140
Heart Rate (bpm)[c]				
	n	4141	1568	5709
	Mean (SD)	73.1 (9.91)	71.4 (10.59)	72.6 (10.13)
	Median	72.0	71.0	72.0
	Min, Max	0, 142	0, 130	0, 142

[a] One enrolled patient in the Retacrit group has missing birth date information. Age for treatment group SILAPO is not included in the data transfer.
[b] Subjects with RACE = Other: European are counted as Caucasian.
[c] Heart Rate = 0 was documented for 2 subjects: Uk-001-0001 in the Retacrit group and De-086-B021 in the Silpao group. For both subjects it was confirmed that heart rate was not assessed.
PFIZER CONFIDENTIAL Source Data: Appendix 7.4 Date of Table Generation: 22FEB2021 (17:21)

System Organ Class Preferred Term Type or Stage	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Number of Subjects with at least one condition	4312	1814	6126
CARDIAC DISORDERS	1825 (40.55)	1040 (56.37)	2865 (45.15)
Atrial fibrillation	564 (12.53)	402 (21.79)	966 (15.22)
Cardiac failure	6 (0.13)	11 (0.60)	17 (0.27)
Cardiac failure chronic	716 (15.91)	531 (28.78)	1247 (19.65)
Stage I	76 (1.69)	69 (3.74)	145 (2.28)
Stage II	389 (8.64)	230 (12.47)	619 (9.75)
Stage III	228 (5.07)	202 (10.95)	430 (6.78)
Stage IV	23 (0.51)	30 (1.63)	53 (0.84)
Coronary artery disease	1144 (25.42)	686 (37.18)	1830 (28.84)
Myocardial infarction	465 (10.33)	267 (14.47)	732 (11.53)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	1 (0.02)	0	1 (0.02)
Unevaluable event	1 (0.02)	0	1 (0.02)
METABOLISM AND NUTRITION DISORDERS	2434 (54.08)	1229 (66.61)	3663 (57.72)
Diabetes mellitus	0	8 (0.43)	8 (0.13)
Hyperlipidaemia	1183 (26.28)	772 (41.84)	1955 (30.81)
Type 1 diabetes mellitus	89 (1.98)	49 (2.66)	138 (2.17)
Type 2 diabetes mellitus	1742 (38.70)	822 (44.55)	2564 (40.40)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	506 (11.24)	322 (17.45)	828 (13.05)
Acute myeloid leukaemia	1 (0.02)	0	1 (0.02)
Adenocarcinoma of colon	3 (0.07)	0	3 (0.05)
Ampullary polyp	1 (0.02)	0	1 (0.02)
Anal cancer	1 (0.02)	0	1 (0.02)
B-cell lymphoma	4 (0.09)	0	4 (0.06)
Basal cell carcinoma	11 (0.24)	0	11 (0.17)
Bladder cancer	55 (1.22)	0	55 (0.87)
Bladder transitional cell carcinoma	1 (0.02)	0	1 (0.02)
Bowen's disease	1 (0.02)	0	1 (0.02)
Breast cancer	57 (1.27)	0	57 (0.90)
Bronchial carcinoma	1 (0.02)	0	1 (0.02)
Cervix carcinoma	14 (0.31)	0	14 (0.22)
Chronic lymphocytic leukaemia	2 (0.04)	0	2 (0.03)
Colon adenoma	1 (0.02)	0	1 (0.02)
Colon cancer	47 (1.04)	0	47 (0.74)
Colorectal adenocarcinoma	1 (0.02)	0	1 (0.02)
Colorectal cancer	6 (0.13)	0	6 (0.09)
Craniopharyngioma	1 (0.02)	0	1 (0.02)
Endometrial cancer	5 (0.11)	0	5 (0.08)
Gastric cancer	10 (0.22)	0	10 (0.16)
Gastrointestinal carcinoma	1 (0.02)	0	1 (0.02)
Gastrointestinal lymphoma	1 (0.02)	0	1 (0.02)
Glioblastoma	1 (0.02)	0	1 (0.02)
Hepatic cancer	3 (0.07)	0	3 (0.05)
Hepatic neoplasm	2 (0.04)	0	2 (0.03)
Invasive ductal breast carcinoma	1 (0.02)	0	1 (0.02)
Kaposi's sarcoma	1 (0.02)	0	1 (0.02)
Laryngeal cancer	6 (0.13)	0	6 (0.09)
Light chain disease	1 (0.02)	0	1 (0.02)
Lip neoplasm malignant stage unspecified	1 (0.02)	0	1 (0.02)
Lip squamous cell carcinoma	1 (0.02)	0	1 (0.02)

System Organ Class Preferred Term Type or Stage	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Lung adenocarcinoma	1 (0.02)	0	1 (0.02)
Lung neoplasm	1 (0.02)	0	1 (0.02)
Lung neoplasm malignant	10 (0.22)	0	10 (0.16)
Lymphoma	3 (0.07)	0	3 (0.05)
Malignant melanoma	3 (0.07)	0	3 (0.05)
Malignant polyp	1 (0.02)	0	1 (0.02)
Marginal zone lymphoma	1 (0.02)	0	1 (0.02)
Meningioma	2 (0.04)	0	2 (0.03)
Metastatic neoplasm	1 (0.02)	0	1 (0.02)
Nasal cavity cancer	1 (0.02)	0	1 (0.02)
Neoplasm malignant	0	322 (17.45)	322 (5.07)
Nephroblastoma	1 (0.02)	0	1 (0.02)
Non-Hodgkin's lymphoma	4 (0.09)	0	4 (0.06)
Non-renal cell carcinoma of kidney	1 (0.02)	0	1 (0.02)
Non-small cell lung cancer	1 (0.02)	0	1 (0.02)
Oesophageal carcinoma	1 (0.02)	0	1 (0.02)
Ovarian cancer	7 (0.16)	0	7 (0.11)
Pancreatic carcinoma	2 (0.04)	0	2 (0.03)
Papillary cystadenoma lymphomatosum	1 (0.02)	0	1 (0.02)
Paraganglion neoplasm	1 (0.02)	0	1 (0.02)
Pharyngeal cancer	1 (0.02)	0	1 (0.02)
Plasma cell myeloma	20 (0.44)	0	20 (0.32)
Plasmacytoma	6 (0.13)	0	6 (0.09)
Prostate cancer	119 (2.64)	0	119 (1.88)
Rectal cancer	9 (0.20)	0	9 (0.14)
Renal cancer	36 (0.80)	0	36 (0.57)
Renal cell carcinoma	14 (0.31)	0	14 (0.22)
Renal neoplasm	4 (0.09)	0	4 (0.06)
Skin cancer	7 (0.16)	0	7 (0.11)
Squamous cell carcinoma	4 (0.09)	0	4 (0.06)
T-cell lymphoma	1 (0.02)	0	1 (0.02)
Testicular seminoma (pure)	1 (0.02)	0	1 (0.02)
Testicular yolk sac tumour	1 (0.02)	0	1 (0.02)
Testis cancer	4 (0.09)	0	4 (0.06)
Thymoma	1 (0.02)	0	1 (0.02)
Thyroid cancer	2 (0.04)	0	2 (0.03)
Tonsil cancer	1 (0.02)	0	1 (0.02)
Transitional cell cancer of the renal pelvis and ureter	1 (0.02)	0	1 (0.02)
Transitional cell carcinoma	9 (0.20)	0	9 (0.14)
Urinary tract carcinoma in situ	1 (0.02)	0	1 (0.02)
Uterine cancer	7 (0.16)	0	7 (0.11)
Vulval cancer	2 (0.04)	0	2 (0.03)
NERVOUS SYSTEM DISORDERS	453 (10.06)	298 (16.15)	751 (11.83)
Cerebrovascular accident	233 (5.18)	182 (9.86)	415 (6.54)
Cerebrovascular disorder	188 (4.18)	174 (9.43)	362 (5.70)
Transient ischaemic attack	113 (2.51)	67 (3.63)	180 (2.84)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	49 (1.09)	49 (2.66)	98 (1.54)
Pulmonary embolism	49 (1.09)	49 (2.66)	98 (1.54)
SOCIAL CIRCUMSTANCES	924 (20.53)	712 (38.59)	1636 (25.78)
Ex-tobacco user	624 (13.86)	522 (28.29)	1146 (18.06)
Ex-smoker	624 (13.86)	522 (28.29)	1146 (18.06)
Tobacco user	300 (6.67)	190 (10.30)	490 (7.72)

System Organ Class Preferred Term Type or Stage	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Current smoker	299 (6.64)	190 (10.30)	489 (7.71)
Missing	1 (0.02)	0	1 (0.02)
VASCULAR DISORDERS	3828 (85.05)	1690 (91.60)	5518 (86.95)
Deep vein thrombosis	77 (1.71)	91 (4.93)	168 (2.65)
Embolism venous	75 (1.67)	113 (6.12)	188 (2.96)
Hypertension	3752 (83.36)	1657 (89.81)	5409 (85.23)
Peripheral arterial occlusive disease	452 (10.04)	342 (18.54)	794 (12.51)

System Organ Class Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Number of Subjects with at least one condition	4500	1843	6343
BLOOD AND LYMPHATIC SYSTEM DISORDERS	2 (0.04)	0	2 (0.03)
Haemolytic uraemic syndrome	1 (0.02)	0	1 (0.02)
Thrombotic thrombocytopenic purpura	1 (0.02)	0	1 (0.02)
CARDIAC DISORDERS	39 (0.87)	0	39 (0.61)
Cardiac disorder	1 (0.02)	0	1 (0.02)
Cardiac failure	4 (0.09)	0	4 (0.06)
Cardiac failure congestive	1 (0.02)	0	1 (0.02)
Cardiorenal syndrome	32 (0.71)	0	32 (0.50)
Coronary artery disease	1 (0.02)	0	1 (0.02)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	174 (3.87)	0	174 (2.74)
Alagille syndrome	1 (0.02)	0	1 (0.02)
Alport's syndrome	6 (0.13)	0	6 (0.09)
Congenital cystic kidney disease	144 (3.20)	0	144 (2.27)
Congenital megaureter	1 (0.02)	0	1 (0.02)
Denys-Drash syndrome	1 (0.02)	0	1 (0.02)
Ectopic kidney	1 (0.02)	0	1 (0.02)
Joubert syndrome	1 (0.02)	0	1 (0.02)
Kidney malformation	6 (0.13)	0	6 (0.09)
Polycystic liver disease	1 (0.02)	0	1 (0.02)
Renal aplasia	1 (0.02)	0	1 (0.02)
Renal dysplasia	5 (0.11)	0	5 (0.08)
Renal hypoplasia	5 (0.11)	0	5 (0.08)
Tuberous sclerosis complex	2 (0.04)	0	2 (0.03)
ENDOCRINE DISORDERS	1 (0.02)	0	1 (0.02)
Hyperparathyroidism	1 (0.02)	0	1 (0.02)
GASTROINTESTINAL DISORDERS	5 (0.11)	0	5 (0.08)
Crohn's disease	1 (0.02)	0	1 (0.02)
Retroperitoneal fibrosis	4 (0.09)	0	4 (0.06)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	307 (6.82)	0	307 (4.84)
Multiple organ dysfunction syndrome	2 (0.04)	0	2 (0.03)
Unevaluable event	305 (6.78)	0	305 (4.81)
HEPATOBILIARY DISORDERS	17 (0.38)	0	17 (0.27)
Chronic hepatitis	1 (0.02)	0	1 (0.02)
Hepatorenal syndrome	14 (0.31)	0	14 (0.22)
Liver disorder	2 (0.04)	0	2 (0.03)
IMMUNE SYSTEM DISORDERS	12 (0.27)	0	12 (0.19)
Amyloidosis	5 (0.11)	0	5 (0.08)
Anti-neutrophil cytoplasmic antibody positive vasculitis	4 (0.09)	0	4 (0.06)
Chronic allograft nephropathy	1 (0.02)	0	1 (0.02)
Kidney transplant rejection	1 (0.02)	0	1 (0.02)
Primary amyloidosis	1 (0.02)	0	1 (0.02)
INFECTIONS AND INFESTATIONS	225 (5.00)	0	225 (3.55)
Legionella infection	1 (0.02)	0	1 (0.02)
Peritonitis	1 (0.02)	0	1 (0.02)

System Organ Class Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Pyelonephritis	95 (2.11)	0	95 (1.50)
Pyelonephritis chronic	121 (2.69)	0	121 (1.91)
Renal tuberculosis	2 (0.04)	0	2 (0.03)
Sepsis	1 (0.02)	0	1 (0.02)
Urinary tract infection	4 (0.09)	0	4 (0.06)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	11 (0.24)	0	11 (0.17)
Complications of transplanted kidney	2 (0.04)	0	2 (0.03)
Gastrointestinal procedural complication	1 (0.02)	0	1 (0.02)
Injury	1 (0.02)	0	1 (0.02)
Overdose	1 (0.02)	0	1 (0.02)
Postoperative renal failure	1 (0.02)	0	1 (0.02)
Procedural haemorrhage	1 (0.02)	0	1 (0.02)
Toxicity to various agents	3 (0.07)	0	3 (0.05)
Transplant failure	1 (0.02)	0	1 (0.02)
INVESTIGATIONS	1 (0.02)	0	1 (0.02)
Glomerular filtration rate increased	1 (0.02)	0	1 (0.02)
METABOLISM AND NUTRITION DISORDERS	6 (0.13)	0	6 (0.09)
Dehydration	2 (0.04)	0	2 (0.03)
Diabetes mellitus	1 (0.02)	0	1 (0.02)
Gout	1 (0.02)	0	1 (0.02)
Hyperkalaemia	1 (0.02)	0	1 (0.02)
Hyperuricaemia	1 (0.02)	0	1 (0.02)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (0.18)	0	8 (0.13)
Collagen disorder	1 (0.02)	0	1 (0.02)
Scleroderma	2 (0.04)	0	2 (0.03)
Sjogren's syndrome	2 (0.04)	0	2 (0.03)
Systemic lupus erythematosus	3 (0.07)	0	3 (0.05)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	32 (0.71)	0	32 (0.50)
Bladder cancer	2 (0.04)	0	2 (0.03)
Hypergammaglobulinaemia benign monoclonal	1 (0.02)	0	1 (0.02)
Monoclonal gammopathy	1 (0.02)	0	1 (0.02)
Myelodysplastic syndrome	1 (0.02)	0	1 (0.02)
Neoplasm malignant	2 (0.04)	0	2 (0.03)
Plasma cell myeloma	10 (0.22)	0	10 (0.16)
Plasmacytoma	3 (0.07)	0	3 (0.05)
Prostate cancer	2 (0.04)	0	2 (0.03)
Renal cancer	1 (0.02)	0	1 (0.02)
Renal cell carcinoma	4 (0.09)	0	4 (0.06)
Renal neoplasm	4 (0.09)	0	4 (0.06)
Transitional cell carcinoma	1 (0.02)	0	1 (0.02)
NERVOUS SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Cerebrovascular insufficiency	1 (0.02)	0	1 (0.02)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	2 (0.04)	0	2 (0.03)
Pre-eclampsia	2 (0.04)	0	2 (0.03)
PSYCHIATRIC DISORDERS	1 (0.02)	0	1 (0.02)
Drug abuse	1 (0.02)	0	1 (0.02)

System Organ Class Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
RENAL AND URINARY DISORDERS	3600 (79.98)	1188 (64.39)	4788 (75.45)
Acute kidney injury	13 (0.29)	0	13 (0.20)
Bladder obstruction	1 (0.02)	0	1 (0.02)
Calculus urinary	2 (0.04)	0	2 (0.03)
Chronic kidney disease	47 (1.04)	0	47 (0.74)
Crystal nephropathy	1 (0.02)	0	1 (0.02)
Diabetic nephropathy	1167 (25.93)	443 (24.01)	1610 (25.37)
Diffuse mesangial sclerosis	1 (0.02)	0	1 (0.02)
Fibrillary glomerulonephritis	1 (0.02)	0	1 (0.02)
Focal segmental glomerulosclerosis	8 (0.18)	0	8 (0.13)
Glomerulonephritis	491 (10.91)	205 (11.11)	696 (10.97)
Glomerulonephritis chronic	1 (0.02)	0	1 (0.02)
Glomerulosclerosis	7 (0.16)	0	7 (0.11)
Goodpasture's syndrome	1 (0.02)	0	1 (0.02)
Hydronephrosis	3 (0.07)	0	3 (0.05)
Hypertensive nephropathy	1409 (31.30)	540 (29.27)	1949 (30.71)
IgA nephropathy	5 (0.11)	0	5 (0.08)
Intercapillary glomerulosclerosis	1 (0.02)	0	1 (0.02)
Ischaemic nephropathy	2 (0.04)	0	2 (0.03)
Kidney congestion	2 (0.04)	0	2 (0.03)
Kidney fibrosis	2 (0.04)	0	2 (0.03)
Kidney small	5 (0.11)	0	5 (0.08)
Lupus nephritis	3 (0.07)	0	3 (0.05)
Myeloma cast nephropathy	3 (0.07)	0	3 (0.05)
Nephritis	2 (0.04)	0	2 (0.03)
Nephroangiosclerosis	42 (0.93)	0	42 (0.66)
Nephrocalcinosis	3 (0.07)	0	3 (0.05)
Nephrolithiasis	19 (0.42)	0	19 (0.30)
Nephropathy	68 (1.51)	0	68 (1.07)
Nephropathy toxic	25 (0.56)	0	25 (0.39)
Nephrosclerosis	113 (2.51)	0	113 (1.78)
Nephrotic syndrome	5 (0.11)	0	5 (0.08)
Obstructive nephropathy	15 (0.33)	0	15 (0.24)
Postrenal failure	2 (0.04)	0	2 (0.03)
Proteinuria	1 (0.02)	0	1 (0.02)
Reflux nephropathy	5 (0.11)	0	5 (0.08)
Renal artery stenosis	7 (0.16)	0	7 (0.11)
Renal atrophy	10 (0.22)	0	10 (0.16)
Renal cortical necrosis	1 (0.02)	0	1 (0.02)
Renal cyst	14 (0.31)	0	14 (0.22)
Renal embolism	2 (0.04)	0	2 (0.03)
Renal failure	11 (0.24)	0	11 (0.17)
Renal hypertension	1 (0.02)	0	1 (0.02)
Renal impairment	1 (0.02)	0	1 (0.02)
Renal mass	1 (0.02)	0	1 (0.02)
Renal tubular disorder	10 (0.22)	0	10 (0.16)
Renal tubular necrosis	2 (0.04)	0	2 (0.03)
Renal vasculitis	1 (0.02)	0	1 (0.02)
Single functional kidney	6 (0.13)	0	6 (0.09)
Tubulointerstitial nephritis	60 (1.33)	0	60 (0.95)
Urate nephropathy	6 (0.13)	0	6 (0.09)
Urinary retention	1 (0.02)	0	1 (0.02)
Urinary tract disorder	3 (0.07)	0	3 (0.05)
Urinary tract obstruction	25 (0.56)	0	25 (0.39)

System Organ Class Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Vesicoureteric reflux	4 (0.09)	0	4 (0.06)
SURGICAL AND MEDICAL PROCEDURES	46 (1.02)	0	46 (0.72)
Chemotherapy	3 (0.07)	0	3 (0.05)
Diuretic therapy	1 (0.02)	0	1 (0.02)
Immunosuppressant drug therapy	1 (0.02)	0	1 (0.02)
Leg amputation	1 (0.02)	0	1 (0.02)
Nephrectomy	27 (0.60)	0	27 (0.43)
Nephroureterectomy	1 (0.02)	0	1 (0.02)
Renal transplant	12 (0.27)	0	12 (0.19)
VASCULAR DISORDERS	69 (1.53)	0	69 (1.09)
Angiosclerosis	1 (0.02)	0	1 (0.02)
Aortic aneurysm	2 (0.04)	0	2 (0.03)
Aortic rupture	1 (0.02)	0	1 (0.02)
Arteriosclerosis	41 (0.91)	0	41 (0.65)
Granulomatosis with polyangiitis	3 (0.07)	0	3 (0.05)
Hypertension	5 (0.11)	0	5 (0.08)
Microscopic polyangiitis	2 (0.04)	0	2 (0.03)
Peripheral vascular disease	1 (0.02)	0	1 (0.02)
Polyarteritis nodosa	1 (0.02)	0	1 (0.02)
Renovascular hypertension	2 (0.04)	0	2 (0.03)
Vasculitis	10 (0.22)	0	10 (0.16)
Vasculitis necrotising	1 (0.02)	0	1 (0.02)
UNCODED	1 (0.02)	655 (35.50)	656 (10.34)
Renal disorders (excl nephropathies)	1 (0.02)	0	1 (0.02)
Uncoded	0	655 (35.50)	655 (10.32)

System Organ Class Preferred Term	Statistic	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
Subject on Dialysis Prior to Study Entry?				
Yes	n (%)	1236 (27.46)	1038 (56.26)	2274 (35.83)
No	n (%)	3265 (72.54)	805 (43.63)	4070 (64.13)
Average Frequency of Dialysis per Week	n	1235	1033	2268
	Mean (SD)	3.1 (0.97)	3.0 (0.50)	3.1 (0.79)
	Median	3.0	3.0	3.0
	Min, Max	1, 7	0, 7	0, 7

ATC 3 Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
OTHER ANTIANEMIC PREPARATIONS	2870 (63.76)	1075 (58.27)	3945 (62.17)
ABSEAMED	21 (0.47)	0	21 (0.33)
ARANESP	144 (3.20)	0	144 (2.27)
BINOCRIT	4 (0.09)	0	4 (0.06)
CERA	5 (0.11)	0	5 (0.08)
DARBEPOETIN ALFA	248 (5.51)	0	248 (3.91)
DARBEPOETINA ALFA	11 (0.24)	0	11 (0.17)
EBOETIN	0	1 (0.05)	1 (0.02)
EBOETIN ZETA	0	1 (0.05)	1 (0.02)
EOETIN ZETA	0	1 (0.05)	1 (0.02)
EOP ZETA	0	1 (0.05)	1 (0.02)
EOPETIN ZETA	0	2 (0.11)	2 (0.03)
EPEOTIN ZETA	0	2 (0.11)	2 (0.03)
EPETIN TETA	0	1 (0.05)	1 (0.02)
EPETIN ZETA	0	2 (0.11)	2 (0.03)
EPO ZETA	0	33 (1.79)	33 (0.52)
EPO [ERYTHROPOIETIN]	67 (1.49)	0	67 (1.06)
EPOEETINZETA	0	1 (0.05)	1 (0.02)
EPOEITN ZETA	0	2 (0.11)	2 (0.03)
EPOERIN-ZETA	0	1 (0.05)	1 (0.02)
EPOETHIN ZETA	0	3 (0.16)	3 (0.05)
EPOETI9N ZETA	0	1 (0.05)	1 (0.02)
EPOETIN	10 (0.22)	25 (1.36)	35 (0.55)
EPOETIN ZETA	0	2 (0.11)	2 (0.03)
EPOETIN ALFA	180 (4.00)	0	180 (2.84)
EPOETIN ALFA HEXAL	0	1 (0.05)	1 (0.02)
EPOETIN ALPHA	0	7 (0.38)	7 (0.11)
EPOETIN BETA	207 (4.60)	0	207 (3.26)
EPOETIN DELTA	4 (0.09)	0	4 (0.06)
EPOETIN THETA	80 (1.78)	0	80 (1.26)
EPOETIN ZEAT	0	1 (0.05)	1 (0.02)
EPOETIN ZET	0	1 (0.05)	1 (0.02)
EPOETIN ZETA	14 (0.31)	850 (46.07)	864 (13.61)
EPOETIN ZETA EPOETIN ZETA	0	1 (0.05)	1 (0.02)
EPOETIN-ZETA	0	3 (0.16)	3 (0.05)
EPOETINA ALFA	9 (0.20)	0	9 (0.14)
EPOETINA BETA	7 (0.16)	0	7 (0.11)
EPOETINN ZETA	0	1 (0.05)	1 (0.02)
EPOETINZETA	0	1 (0.05)	1 (0.02)
EPOETOIN ZETA	0	1 (0.05)	1 (0.02)
EPOIETIN ZETA	0	8 (0.43)	8 (0.13)
EPOITIN	0	3 (0.16)	3 (0.05)
EPOITIN ZETA	0	7 (0.38)	7 (0.11)
EPORATIO	4 (0.09)	0	4 (0.06)
EPORTIN ZETA	0	2 (0.11)	2 (0.03)
EPOTEIN ZETA	0	3 (0.16)	3 (0.05)
EPOTEIN-ZETA	0	1 (0.05)	1 (0.02)
EPOTIN ZETA	0	1 (0.05)	1 (0.02)
EPREX	29 (0.64)	0	29 (0.46)
ERYPO [EPOETIN ALFA]	6 (0.13)	0	6 (0.09)
ERYPOETIN	0	1 (0.05)	1 (0.02)
ERYPOETIN ZETA	0	2 (0.11)	2 (0.03)
ERYPROETIN	0	2 (0.11)	2 (0.03)
ERYPROTEIN ZETA	0	1 (0.05)	1 (0.02)
ERYTHROPEITIN ZETA	0	3 (0.16)	3 (0.05)
ERYTHROPEOITIN ZETA	0	1 (0.05)	1 (0.02)

ATC 3 Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
ERYTHROPOEITIN	0	2 (0.11)	2 (0.03)
ERYTHROPOEITIN ZETA	0	43 (2.33)	43 (0.68)
ERYTHROPOETIN	0	3 (0.16)	3 (0.05)
ERYTHROPOETIN (EPOETIN ZETA)	0	1 (0.05)	1 (0.02)
ERYTHROPOETIN ZETA	0	14 (0.76)	14 (0.22)
ERYTHROPOETIN [EPOETIN ALFA]	13 (0.29)	0	13 (0.20)
ERYTHROPOETIN [EPOETIN BETA]	21 (0.47)	0	21 (0.33)
ERYTHROPOETN ZETA	0	1 (0.05)	1 (0.02)
ERYTHROPOIETIN	0	7 (0.38)	7 (0.11)
ERYTHROPOIETIN ZETA	0	12 (0.65)	12 (0.19)
ERYTHRPOEITIN ZETA	0	1 (0.05)	1 (0.02)
ERYTROPOEITIN ZETA	0	1 (0.05)	1 (0.02)
EYTHROPEITIN ZETA	0	1 (0.05)	1 (0.02)
METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA	120 (2.67)	0	120 (1.89)
MIRCERA	22 (0.49)	0	22 (0.35)
NEO RECORMON	19 (0.42)	0	19 (0.30)
NESPO	2 (0.04)	0	2 (0.03)
RECORMON [EPOETIN BETA]	5 (0.11)	0	5 (0.08)
RETACRIT	0	1 (0.05)	1 (0.02)
RETACRIT [EPOETIN ZETA]	2216 (49.23)	0	2216 (34.92)
SILAPO	1 (0.02)	6 (0.33)	7 (0.11)
Uncoded	0	1 (0.05)	1 (0.02)
UNCODED	3 (0.07)	334 (18.10)	337 (5.31)
ALPHA	0	1 (0.05)	1 (0.02)
ARANESP	0	1 (0.05)	1 (0.02)
BETA	0	1 (0.05)	1 (0.02)
BINOCRIT	0	1 (0.05)	1 (0.02)
DARB EPOETHIN	0	1 (0.05)	1 (0.02)
DARBAPOETIN	0	5 (0.27)	5 (0.08)
DARBEPOETEIN ALPHA	0	1 (0.05)	1 (0.02)
DARBEPOETIN	0	20 (1.08)	20 (0.32)
DARBEPOETIN ALFA	0	1 (0.05)	1 (0.02)
DARBEPOETIN ALFA	0	25 (1.36)	25 (0.39)
DARBEPOETIN ALPHA	0	9 (0.49)	9 (0.14)
DARBEPOIETIN	0	1 (0.05)	1 (0.02)
DARBEPOITIN	0	1 (0.05)	1 (0.02)
DARBEPORIN ALFA	0	1 (0.05)	1 (0.02)
DARBEPOTIN ALFA	0	1 (0.05)	1 (0.02)
DARBOPOETIN	0	1 (0.05)	1 (0.02)
DARBPOETIN ALPHA	0	4 (0.22)	4 (0.06)
DAREPOETIN ALPHA	0	5 (0.27)	5 (0.08)
EOPOETIN ALPHA	0	1 (0.05)	1 (0.02)
EPAETIN ALFA HEXAL	0	1 (0.05)	1 (0.02)
EPO ALFA	0	16 (0.87)	16 (0.25)
EPO BETA	0	2 (0.11)	2 (0.03)
EPOETHIN BETA	0	1 (0.05)	1 (0.02)
EPOETHIN THETA	0	1 (0.05)	1 (0.02)
EPOETIN	0	28 (1.52)	28 (0.44)
EPOETIN BETA	0	1 (0.05)	1 (0.02)
EPOETIN ALFA	0	26 (1.41)	26 (0.41)
EPOETIN ALFA HEXAL	0	1 (0.05)	1 (0.02)
EPOETIN ALPHA	0	83 (4.50)	83 (1.31)
EPOETIN ALPHA HEXAL	0	1 (0.05)	1 (0.02)
EPOETIN BETA	0	38 (2.06)	38 (0.60)
EPOETIN DARB	0	1 (0.05)	1 (0.02)
EPOETIN THETA	0	21 (1.14)	21 (0.33)

ATC 3 Preferred Term	Retacrit (N = 4501) n(%)	Silapo (N = 1845) n(%)	Total (N = 6346) n(%)
EPOETIN ZETA	0	2 (0.11)	2 (0.03)
EPOETIN-BETA	0	2 (0.11)	2 (0.03)
EPOTEIN ALFA	0	1 (0.05)	1 (0.02)
EPOTEIN ALPHA	0	2 (0.11)	2 (0.03)
EPOTETIN BETA	0	1 (0.05)	1 (0.02)
ERYPO	0	1 (0.05)	1 (0.02)
ERYPO ALFA	0	1 (0.05)	1 (0.02)
ERYPOPOETIN	0	1 (0.05)	1 (0.02)
ERYTHROPOETIN ALPHA	0	1 (0.05)	1 (0.02)
ERYTHROPOETIN BETA	0	1 (0.05)	1 (0.02)
ERYTHROPOIETIN	0	1 (0.05)	1 (0.02)
ERYTHROPOIETIN BETA	0	1 (0.05)	1 (0.02)
ERYTHROPROTEIN	0	1 (0.05)	1 (0.02)
METHOXY-POLYETHYLENGLYCOL-EPOETIN BETA	0	2 (0.11)	2 (0.03)
METHOXY-POLYETHYLENGLYOL-EPOETIN BETA	0	1 (0.05)	1 (0.02)
PEG EPOETIN BETA	0	4 (0.22)	4 (0.06)
PEG-EPOETIN BETA	0	3 (0.16)	3 (0.05)
PEG-EPOETIN ZETA	0	1 (0.05)	1 (0.02)
PEG-EPOETIN-BETA	0	1 (0.05)	1 (0.02)
UNBEKANNT	0	1 (0.05)	1 (0.02)
Uncoded	3 (0.07)	3 (0.16)	6 (0.09)

Number of Subjects Evaluable for Adverse Events	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects Discontinued Due to AE	125 (2.78)	119 (6.46)	244 (3.85)
Number of Events Leading to Discontinuation	163	159	322
Number of Subjects Discontinued Due to AESI	114 (2.54)	113 (6.14)	227 (3.58)
Number of Subjects Discontinued Due to ADRs other than AESIs	11 (0.24)	9 (0.49)	20 (0.32)
Number of Subjects Discontinued Due to Fatal AEs	70 (1.56)	73 (3.97)	143 (2.26)
Blood and lymphatic system disorders	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
Cardiac disorders	62 (1.38)	49 (2.66)	111 (1.75)
Acute myocardial infarction	25 (0.56)	2 (0.11)	27 (0.43)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Myocardial infarction	35 (0.78)	48 (2.61)	83 (1.31)
Palpitations	1 (0.02)	0	1 (0.02)
Eye disorders	1 (0.02)	2 (0.11)	3 (0.05)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	1 (0.05)	1 (0.02)
Gastrointestinal disorders	2 (0.04)	3 (0.16)	5 (0.08)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Lip swelling	1 (0.02)	0	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
Nausea	1 (0.02)	0	1 (0.02)
Swollen tongue	1 (0.02)	0	1 (0.02)
General disorders and administration site conditions	6 (0.13)	8 (0.43)	14 (0.22)
Drug ineffective	2 (0.04)	8 (0.43)	10 (0.16)
Influenza like illness	1 (0.02)	0	1 (0.02)
Malaise	3 (0.07)	0	3 (0.05)
Infections and infestations	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
Injury, poisoning and procedural complications	2 (0.04)	9 (0.49)	11 (0.17)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	6 (0.33)	6 (0.09)
Shunt thrombosis	0	2 (0.11)	2 (0.03)
Subdural haematoma	2 (0.04)	0	2 (0.03)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
Investigations	0	3 (0.16)	3 (0.05)
Haemoglobin decreased	0	3 (0.16)	3 (0.05)
Musculoskeletal and connective tissue disorders	0	1 (0.05)	1 (0.02)
Bone pain	0	1 (0.05)	1 (0.02)

Note: Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.9 Date of Table Generation: 17AUG2020 (13:44)

Number of Subjects Evaluable for Adverse Events	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Nervous system disorders	42 (0.93)	27 (1.47)	69 (1.09)
Basal ganglia haemorrhage	1 (0.02)	0	1 (0.02)
Cerebral haemorrhage	5 (0.11)	6 (0.33)	11 (0.17)
Cerebral infarction	5 (0.11)	0	5 (0.08)
Cerebral ischaemia	2 (0.04)	0	2 (0.03)
Cerebrovascular accident	18 (0.40)	2 (0.11)	20 (0.32)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Dizziness	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Headache	3 (0.07)	0	3 (0.05)
Ischaemic stroke	5 (0.11)	15 (0.81)	20 (0.32)
Transient ischaemic attack	3 (0.07)	3 (0.16)	6 (0.09)
Product issues	1 (0.02)	0	1 (0.02)
Thrombosis in device	1 (0.02)	0	1 (0.02)
Psychiatric disorders	1 (0.02)	0	1 (0.02)
Nightmare	1 (0.02)	0	1 (0.02)
Reproductive system and breast disorders	2 (0.04)	0	2 (0.03)
Breast disorder	1 (0.02)	0	1 (0.02)
Vulvovaginal pruritus	1 (0.02)	0	1 (0.02)
Respiratory, thoracic and mediastinal disorders	5 (0.11)	8 (0.43)	13 (0.21)
Pulmonary embolism	5 (0.11)	8 (0.43)	13 (0.21)
Skin and subcutaneous tissue disorders	4 (0.09)	3 (0.16)	7 (0.11)
Dermatitis allergic	1 (0.02)	0	1 (0.02)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
Eczema	0	1 (0.05)	1 (0.02)
Hypertrichosis	0	1 (0.05)	1 (0.02)
Pruritus	2 (0.04)	1 (0.05)	3 (0.05)
Rash	1 (0.02)	0	1 (0.02)
Vascular disorders	18 (0.40)	21 (1.14)	39 (0.62)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	2 (0.11)	2 (0.03)
Arterial thrombosis	1 (0.02)	0	1 (0.02)
Deep vein thrombosis	2 (0.04)	2 (0.11)	4 (0.06)
Embolism	5 (0.11)	0	5 (0.08)
Embolism arterial	0	1 (0.05)	1 (0.02)
Hypertension	1 (0.02)	0	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)
Infarction	1 (0.02)	0	1 (0.02)
Pelvic venous thrombosis	1 (0.02)	0	1 (0.02)
Peripheral arterial occlusive disease	3 (0.07)	12 (0.65)	15 (0.24)
Peripheral artery occlusion	0	1 (0.05)	1 (0.02)

Note: Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.9 Date of Table Generation: 17AUG2020 (13:44)

Number of Subjects Evaluable for Adverse Events	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	0	1 (0.02)
Thrombophlebitis superficial	1 (0.02)	0	1 (0.02)
Thrombosis	2 (0.04)	0	2 (0.03)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

Note: Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.9 Date of Table Generation: 17AUG2020 (13:44)

Subjects Evaluable for Adverse Events Number of Subjects	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Adverse Events	252	316	568
Subjects Discontinued from Study Due to Adverse Events[a]	125 (2.78)	119 (6.46)	244 (3.85)
Subjects Reporting Death Due to Adverse Events	70 (1.56)	73 (3.97)	143 (2.26)
Subjects with Adverse Events	199 (4.43)	242 (13.15)	441 (6.96)
Subjects with Serious Adverse Events	180 (4.00)	235 (12.76)	415 (6.55)
Subjects with Adverse Events of Special Interest	187 (4.16)	231 (12.55)	418 (6.60)
Subjects with Serious Adverse Events of Special Interest	178 (3.96)	231 (12.55)	409 (6.45)
Subjects with Adverse Drug Reactions other than Events of Special Interest	12 (0.27)	16 (0.87)	28 (0.44)
Subjects with Serious Adverse Drug Reactions other than Events of Special Interest	2 (0.04)	9 (0.49)	11 (0.17)

[a] Subjects who have an AE record that indicates that the AE caused the subject to be discontinued from the study.
Note: The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
There are 5 subjects from Silapo treatment group who had both AESI and ADR reported.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.9 Date of Table Generation: 15MAR2021 (17:10)

Subjects Evaluable for Adverse Events Number of Subjects	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Adverse Events	252	312	564
Subjects Discontinued from Study Due to Adverse Events[a]	125 (2.78)	119 (6.46)	244 (3.85)
Subjects Reporting Death Due to Adverse Events	70 (1.56)	73 (3.97)	143 (2.26)
Subjects with Adverse Events	199 (4.43)	240 (13.04)	439 (6.93)
Subjects with Serious Adverse Events	180 (4.00)	233 (12.66)	413 (6.52)
Subjects with Adverse Events of Special Interest	187 (4.16)	229 (12.44)	416 (6.56)
Subjects with Serious Adverse Events of Special Interest	178 (3.96)	229 (12.44)	407 (6.42)
Subjects with Adverse Drug Reactions other than Events of Special Interest	12 (0.27)	16 (0.87)	28 (0.44)
Subjects with Serious Adverse Drug Reactions other than Events of Special Interest	2 (0.04)	9 (0.49)	11 (0.17)

[a] Subjects who have an AE record that indicates that the AE caused the subject to be discontinued from the study.
Note: The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
There are 5 subjects from Silapo treatment group who had both AESI and ADR reported.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.9 Date of Table Generation: 15MAR2021 (17:27)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One Adverse Event	199 (4.43)	242 (13.15)	441 (6.96)
Number of Adverse Events	252	316	568
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
CARDIAC DISORDERS	88 (1.96)	77 (4.18)	165 (2.60)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Arrhythmia	0	1 (0.05)	1 (0.02)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
Palpitations	1 (0.02)	0	1 (0.02)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	3 (0.07)	5 (0.27)	8 (0.13)
Diarrhoea	1 (0.02)	0	1 (0.02)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Lip swelling	1 (0.02)	0	1 (0.02)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
Nausea	1 (0.02)	1 (0.05)	2 (0.03)
Swollen tongue	1 (0.02)	0	1 (0.02)
Vomiting	0	1 (0.05)	1 (0.02)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	16 (0.36)	22 (1.20)	38 (0.60)
Drug ineffective	12 (0.27)	21 (1.14)	33 (0.52)
Influenza like illness	1 (0.02)	0	1 (0.02)
Malaise	3 (0.07)	0	3 (0.05)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)

The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:48)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased	0	5 (0.27)	5 (0.08)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	1 (0.05)	1 (0.02)
Bone pain	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	66 (1.47)	53 (2.88)	119 (1.88)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	7 (0.16)	1 (0.05)	8 (0.13)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Dizziness	1 (0.02)	1 (0.05)	2 (0.03)
Dyskinesia	0	1 (0.05)	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Headache	3 (0.07)	0	3 (0.05)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Somnolence	0	1 (0.05)	1 (0.02)
Transient ischaemic attack	8 (0.18)	10 (0.54)	18 (0.28)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
PSYCHIATRIC DISORDERS	1 (0.02)	0	1 (0.02)
Nightmare	1 (0.02)	0	1 (0.02)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (0.04)	0	2 (0.03)
Breast disorder	1 (0.02)	0	1 (0.02)
Vulvovaginal pruritus	1 (0.02)	0	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	4 (0.09)	5 (0.27)	9 (0.14)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis allergic	1 (0.02)	1 (0.05)	2 (0.03)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
Eczema	0	1 (0.05)	1 (0.02)

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Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:48)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Hypertrichosis	0	1 (0.05)	1 (0.02)
Pruritus	2 (0.04)	1 (0.05)	3 (0.05)
Rash	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	38 (0.85)	47 (2.55)	85 (1.34)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	12 (0.27)	0	12 (0.19)
Embolism arterial	0	1 (0.05)	1 (0.02)
Hypertension	1 (0.02)	0	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:48)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One Serious Adverse Event	180 (4.00)	235 (12.76)	415 (6.55)
Number of Serious Adverse Events	221	308	529
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
CARDIAC DISORDERS	87 (1.94)	77 (4.18)	164 (2.59)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Arrhythmia	0	1 (0.05)	1 (0.02)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	1 (0.02)	4 (0.22)	5 (0.08)
Diarrhoea	1 (0.02)	0	1 (0.02)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.09)	22 (1.20)	26 (0.41)
Drug ineffective	4 (0.09)	21 (1.14)	25 (0.39)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased	0	5 (0.27)	5 (0.08)
NERVOUS SYSTEM DISORDERS	61 (1.36)	52 (2.82)	113 (1.78)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)

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Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
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Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	6 (0.13)	1 (0.05)	7 (0.11)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Dizziness	0	1 (0.05)	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Somnolence	0	1 (0.05)	1 (0.02)
Transient ischaemic attack	7 (0.16)	10 (0.54)	17 (0.27)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	36 (0.80)	47 (2.55)	83 (1.31)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	11 (0.24)	0	11 (0.17)
Embolism arterial	0	1 (0.05)	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)

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Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:49)

Number of Subjects Evaluable for AEs Number of Subjects by AESI System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One Adverse Event of Special Interest	187 (4.16)	231 (12.55)	418 (6.60)
Number of Adverse Event of Special Interests	230	297	527
Lack of Efficacy	12 (0.27)	22 (1.20)	34 (0.54)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	12 (0.27)	22 (1.20)	34 (0.54)
Drug ineffective	12 (0.27)	21 (1.14)	33 (0.52)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
Pure Red Cell Aplasia	1 (0.02)	0	1 (0.02)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
Thromboembolic Events	176 (3.91)	213 (11.57)	389 (6.14)
CARDIAC DISORDERS	87 (1.94)	76 (4.13)	163 (2.57)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	0	4 (0.22)	4 (0.06)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	63 (1.40)	51 (2.77)	114 (1.80)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	7 (0.16)	1 (0.05)	8 (0.13)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)

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MedDRA v23 coding dictionary was applied.
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Number of Subjects Evaluable for AEs Number of Subjects by AESI System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Transient ischaemic attack	8 (0.18)	10 (0.54)	18 (0.28)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	37 (0.82)	46 (2.50)	83 (1.31)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	12 (0.27)	0	12 (0.19)
Embolism arterial	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

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Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
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Number of Subjects Evaluable for AEs Number of Subjects by AESI System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at least one Serious Adverse Event of Special Interest	178 (3.96)	231 (12.55)	409 (6.45)
Number of Serious Adverse Event of Special Interests	219	297	516
Lack of Efficacy	4 (0.09)	22 (1.20)	26 (0.41)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.09)	22 (1.20)	26 (0.41)
Drug ineffective	4 (0.09)	21 (1.14)	25 (0.39)
Therapeutic product effect decreased	0	1 (0.05)	1 (0.02)
Pure Red Cell Aplasia	1 (0.02)	0	1 (0.02)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.02)	0	1 (0.02)
Aplasia pure red cell	1 (0.02)	0	1 (0.02)
Thromboembolic Events	174 (3.87)	213 (11.57)	387 (6.11)
CARDIAC DISORDERS	87 (1.94)	76 (4.13)	163 (2.57)
Acute myocardial infarction	44 (0.98)	3 (0.16)	47 (0.74)
Coronary artery occlusion	0	2 (0.11)	2 (0.03)
Coronary artery thrombosis	1 (0.02)	0	1 (0.02)
Intracardiac thrombus	1 (0.02)	0	1 (0.02)
Myocardial infarction	42 (0.93)	72 (3.91)	114 (1.80)
EYE DISORDERS	1 (0.02)	3 (0.16)	4 (0.06)
Retinal artery occlusion	0	1 (0.05)	1 (0.02)
Retinal infarction	1 (0.02)	0	1 (0.02)
Retinal vein thrombosis	0	2 (0.11)	2 (0.03)
GASTROINTESTINAL DISORDERS	0	4 (0.22)	4 (0.06)
Intestinal infarction	0	3 (0.16)	3 (0.05)
Mesenteric artery stenosis	0	1 (0.05)	1 (0.02)
Mesenteric vein thrombosis	0	1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.11)	36 (1.96)	41 (0.65)
Arterial bypass occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula occlusion	0	1 (0.05)	1 (0.02)
Arteriovenous fistula thrombosis	2 (0.04)	0	2 (0.03)
Carotid artery restenosis	0	1 (0.05)	1 (0.02)
Shunt occlusion	0	27 (1.47)	27 (0.43)
Shunt thrombosis	1 (0.02)	8 (0.43)	9 (0.14)
Subdural haematoma	2 (0.04)	1 (0.05)	3 (0.05)
Vascular graft occlusion	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	61 (1.36)	51 (2.77)	112 (1.77)
Basal ganglia haemorrhage	2 (0.04)	0	2 (0.03)
Cerebellar haematoma	0	1 (0.05)	1 (0.02)
Cerebellar infarction	1 (0.02)	0	1 (0.02)
Cerebral artery occlusion	0	1 (0.05)	1 (0.02)
Cerebral haemorrhage	8 (0.18)	6 (0.33)	14 (0.22)
Cerebral infarction	6 (0.13)	1 (0.05)	7 (0.11)
Cerebral ischaemia	3 (0.07)	1 (0.05)	4 (0.06)
Cerebrovascular accident	27 (0.60)	6 (0.33)	33 (0.52)
Cerebrovascular disorder	1 (0.02)	0	1 (0.02)
Embolic cerebral infarction	1 (0.02)	0	1 (0.02)
Embolic stroke	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified AESI that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:50)

Number of Subjects Evaluable for AEs Number of Subjects by AESI System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Haemorrhagic stroke	1 (0.02)	1 (0.05)	2 (0.03)
Hemiparesis	0	1 (0.05)	1 (0.02)
Ischaemic stroke	8 (0.18)	26 (1.41)	34 (0.54)
Transient ischaemic attack	7 (0.16)	10 (0.54)	17 (0.27)
PRODUCT ISSUES	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis in device	1 (0.02)	1 (0.05)	2 (0.03)
RENAL AND URINARY DISORDERS	0	1 (0.05)	1 (0.02)
Renal artery thrombosis	0	1 (0.05)	1 (0.02)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.22)	14 (0.76)	24 (0.38)
Pulmonary embolism	9 (0.20)	14 (0.76)	23 (0.36)
Pulmonary thrombosis	1 (0.02)	0	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	0	1 (0.05)	1 (0.02)
Arterial stent insertion	0	1 (0.05)	1 (0.02)
VASCULAR DISORDERS	36 (0.80)	46 (2.50)	82 (1.29)
Aortic thrombosis	0	1 (0.05)	1 (0.02)
Arterial occlusive disease	0	10 (0.54)	10 (0.16)
Arterial thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Deep vein thrombosis	6 (0.13)	7 (0.38)	13 (0.21)
Embolism	11 (0.24)	0	11 (0.17)
Embolism arterial	0	1 (0.05)	1 (0.02)
Iliac artery occlusion	1 (0.02)	0	1 (0.02)
Infarction	2 (0.04)	0	2 (0.03)
Pelvic venous thrombosis	2 (0.04)	0	2 (0.03)
Peripheral arterial occlusive disease	5 (0.11)	25 (1.36)	30 (0.47)
Peripheral artery occlusion	0	3 (0.16)	3 (0.05)
Peripheral artery thrombosis	1 (0.02)	0	1 (0.02)
Peripheral embolism	1 (0.02)	1 (0.05)	2 (0.03)
Subclavian vein thrombosis	1 (0.02)	1 (0.05)	2 (0.03)
Thrombophlebitis superficial	1 (0.02)	1 (0.05)	2 (0.03)
Thrombosis	5 (0.11)	0	5 (0.08)
Venous occlusion	0	1 (0.05)	1 (0.02)
Venous thrombosis	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified AESI that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:50)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One ADR other than Events of Special Interest	12 (0.27)	16 (0.87)	28 (0.44)
Number of ADRs other than Events of Special Interest	22	19	41
CARDIAC DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Arrhythmia	0	1 (0.05)	1 (0.02)
Palpitations	1 (0.02)	0	1 (0.02)
GASTROINTESTINAL DISORDERS	3 (0.07)	1 (0.05)	4 (0.06)
Diarrhoea	1 (0.02)	0	1 (0.02)
Lip swelling	1 (0.02)	0	1 (0.02)
Nausea	1 (0.02)	1 (0.05)	2 (0.03)
Swollen tongue	1 (0.02)	0	1 (0.02)
Vomiting	0	1 (0.05)	1 (0.02)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.09)	0	4 (0.06)
Influenza like illness	1 (0.02)	0	1 (0.02)
Malaise	3 (0.07)	0	3 (0.05)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased	0	5 (0.27)	5 (0.08)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	0	1 (0.05)	1 (0.02)
Bone pain	0	1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	3 (0.07)	2 (0.11)	5 (0.08)
Dizziness	1 (0.02)	1 (0.05)	2 (0.03)
Dyskinesia	0	1 (0.05)	1 (0.02)
Headache	3 (0.07)	0	3 (0.05)
Somnolence	0	1 (0.05)	1 (0.02)
PSYCHIATRIC DISORDERS	1 (0.02)	0	1 (0.02)
Nightmare	1 (0.02)	0	1 (0.02)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (0.04)	0	2 (0.03)
Breast disorder	1 (0.02)	0	1 (0.02)
Vulvovaginal pruritus	1 (0.02)	0	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	4 (0.09)	5 (0.27)	9 (0.14)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis allergic	1 (0.02)	1 (0.05)	2 (0.03)
Dermatitis atopic	1 (0.02)	0	1 (0.02)

The table only includes protocol-specified ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
Haemoglobin decreased events were finally assessed as ADRs other than AESIs as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:51)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Eczema	0	1 (0.05)	1 (0.02)
Hypertrichosis	0	1 (0.05)	1 (0.02)
Pruritus	2 (0.04)	1 (0.05)	3 (0.05)
Rash	1 (0.02)	0	1 (0.02)
VASCULAR DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Hypertension	1 (0.02)	0	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)

The table only includes protocol-specified ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
Haemoglobin decreased events were finally assessed as ADRs other than AESIs as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:51)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One ADR other than Events of Special Interest	NA	79 (4.29)	79 (1.25)
Number of ADRs other than Events of Special Interest	NA	112	112
BLOOD AND LYMPHATIC SYSTEM DISORDERS	NA	3 (0.16)	3 (0.05)
Anaemia		2 (0.11)	2 (0.03)
Anaemia of malignant disease		1 (0.05)	1 (0.02)
Pancytopenia		1 (0.05)	1 (0.02)
CARDIAC DISORDERS	NA	38 (2.06)	38 (0.60)
Angina pectoris		4 (0.22)	4 (0.06)
Angina unstable		20 (1.09)	20 (0.32)
Atrial fibrillation		5 (0.27)	5 (0.08)
Cardiac arrest		1 (0.05)	1 (0.02)
Cardiac disorder		1 (0.05)	1 (0.02)
Cardiac failure		3 (0.16)	3 (0.05)
Cardiac failure congestive		1 (0.05)	1 (0.02)
Coronary artery disease		4 (0.22)	4 (0.06)
Coronary artery stenosis		1 (0.05)	1 (0.02)
Pericardial effusion		1 (0.05)	1 (0.02)
Tachycardia		1 (0.05)	1 (0.02)
Ventricular arrhythmia		1 (0.05)	1 (0.02)
EYE DISORDERS	NA	1 (0.05)	1 (0.02)
Optic ischaemic neuropathy		1 (0.05)	1 (0.02)
Visual impairment		1 (0.05)	1 (0.02)
GASTROINTESTINAL DISORDERS	NA	7 (0.38)	7 (0.11)
Abdominal hernia		1 (0.05)	1 (0.02)
Acute abdomen		1 (0.05)	1 (0.02)
Colitis ischaemic		1 (0.05)	1 (0.02)
Duodenal ulcer		1 (0.05)	1 (0.02)
Gastrointestinal haemorrhage		2 (0.11)	2 (0.03)
Gastrointestinal necrosis		1 (0.05)	1 (0.02)
Intestinal ischaemia		1 (0.05)	1 (0.02)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	NA	9 (0.49)	9 (0.14)
Asthenia		1 (0.05)	1 (0.02)
Cardiac death		2 (0.11)	2 (0.03)
Death		4 (0.22)	4 (0.06)
General physical health deterioration		1 (0.05)	1 (0.02)
Multiple organ dysfunction syndrome		1 (0.05)	1 (0.02)
Peripheral swelling		1 (0.05)	1 (0.02)

The adverse drug reactions (ADR) included in this table are adverse events with:
1) reporter causality assessment equal to 'UNLIKELY RELATED' or 'NOT ASSESSABLE',
2) reporter causality assessment equal to 'NOT RELATED' and company causality assessment equal to 'POSSIBLE RELATED' (1 event: Gastrointestinal haemorrhage), 'UNLIKELY RELATED' or 'NOT ASSESSABLE', and
3) reported causality assessment equal to 'UNKNOWN' and company causality assessment equal to 'UNLIKELY RELATED'.
In addition to the ADRs listed in table 15.3.3.5, events with the mentioned conditions are also considered to have a reasonable possibility of a causal relationship in PMS-830-09-0082 protocol.
Haemoglobin decreased, Anaemia, Anaemia of malignant disease and Pancytopenia events were finally assessed as ADRs other than AESIs as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:53)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Pyrexia		1 (0.05)	1 (0.02)
INFECTIONS AND INFESTATIONS	NA	8 (0.43)	8 (0.13)
Abscess		1 (0.05)	1 (0.02)
Device related infection		1 (0.05)	1 (0.02)
Gangrene		1 (0.05)	1 (0.02)
Infected bunion		1 (0.05)	1 (0.02)
Peritonitis bacterial		1 (0.05)	1 (0.02)
Pneumonia		2 (0.11)	2 (0.03)
Shunt infection		1 (0.05)	1 (0.02)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	NA	9 (0.49)	9 (0.14)
Arteriovenous fistula site complication		1 (0.05)	1 (0.02)
Peripheral artery restenosis		1 (0.05)	1 (0.02)
Shunt malfunction		1 (0.05)	1 (0.02)
Shunt stenosis		5 (0.27)	5 (0.08)
Wound		1 (0.05)	1 (0.02)
INVESTIGATIONS	NA	4 (0.22)	4 (0.06)
Haemoglobin decreased		4 (0.22)	4 (0.06)
METABOLISM AND NUTRITION DISORDERS	NA	1 (0.05)	1 (0.02)
Hypoglycaemia		1 (0.05)	1 (0.02)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	NA	1 (0.05)	1 (0.02)
Bladder neoplasm		1 (0.05)	1 (0.02)
NERVOUS SYSTEM DISORDERS	NA	4 (0.22)	4 (0.06)
Dysarthria		1 (0.05)	1 (0.02)
Dyskinesia		1 (0.05)	1 (0.02)
Leukoencephalopathy		1 (0.05)	1 (0.02)
Syncope		1 (0.05)	1 (0.02)
PSYCHIATRIC DISORDERS	NA	1 (0.05)	1 (0.02)
Delusion		1 (0.05)	1 (0.02)
RENAL AND URINARY DISORDERS	NA	1 (0.05)	1 (0.02)
Haematuria		1 (0.05)	1 (0.02)
SURGICAL AND MEDICAL PROCEDURES	NA	1 (0.05)	1 (0.02)
Finger amputation		1 (0.05)	1 (0.02)
VASCULAR DISORDERS	NA	11 (0.60)	11 (0.17)
Arterial stenosis		1 (0.05)	1 (0.02)
Extremity necrosis		1 (0.05)	1 (0.02)

The adverse drug reactions (ADR) included in this table are adverse events with:
1) reporter causality assessment equal to 'UNLIKELY RELATED' or 'NOT ASSESSABLE',
2) reporter causality assessment equal to 'NOT RELATED' and company causality assessment equal to 'POSSIBLE RELATED' (1 event: Gastrointestinal haemorrhage), 'UNLIKELY RELATED' or 'NOT ASSESSABLE', and
3) reported causality assessment equal to 'UNKNOWN' and company causality assessment equal to 'UNLIKELY RELATED'.
In addition to the ADRs listed in table 15.3.3.5, events with the mentioned conditions are also considered to have a reasonable possibility of a causal relationship in PMS-830-09-0082 protocol.
Haemoglobin decreased, Anaemia, Anaemia of malignant disease and Pancytopenia events were finally assessed as ADRs other than AESIs as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:53)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Iliac artery stenosis		1 (0.05)	1 (0.02)
Ischaemia		1 (0.05)	1 (0.02)
Peripheral artery aneurysm		1 (0.05)	1 (0.02)
Peripheral artery stenosis		3 (0.16)	3 (0.05)
Peripheral ischaemia		2 (0.11)	2 (0.03)
Venous stenosis		2 (0.11)	2 (0.03)

The adverse drug reactions (ADR) included in this table are adverse events with:
1) reporter causality assessment equal to 'UNLIKELY RELATED' or 'NOT ASSESSABLE',
2) reporter causality assessment equal to 'NOT RELATED' and company causality assessment equal to 'POSSIBLE RELATED' (1 event: Gastrointestinal haemorrhage), 'UNLIKELY RELATED' or 'NOT ASSESSABLE', and
3) reported causality assessment equal to 'UNKNOWN' and company causality assessment equal to 'UNLIKELY RELATED'.
In addition to the ADRs listed in table 15.3.3.5, events with the mentioned conditions are also considered to have a reasonable possibility of a causal relationship in PMS-830-09-0082 protocol.
Haemoglobin decreased, Anaemia, Anaemia of malignant disease and Pancytopenia events were finally assessed as ADRs other than AESIs as other causes than lack of efficacy could be identified and/or PRCA could be excluded.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:53)

Number of Subjects Evaluable for Adverse Events Number of Subjects by System Organ Class and Preferred Term	Retacrit (N = 4496) n(%)	Silapo (N = 1841) n(%)	Total (N = 6337) n(%)
Number of Subjects with at Least One Serious ADR other than Events of Special Interest	2 (0.04)	9 (0.49)	11 (0.17)
Number of Serious ADRs other than Events of Special Interest	2	11	13
CARDIAC DISORDERS	0	1 (0.05)	1 (0.02)
Arrhythmia	0	1 (0.05)	1 (0.02)
GASTROINTESTINAL DISORDERS	1 (0.02)	0	1 (0.02)
Diarrhoea	1 (0.02)	0	1 (0.02)
INFECTIONS AND INFESTATIONS	0	1 (0.05)	1 (0.02)
Gangrene	0	1 (0.05)	1 (0.02)
INVESTIGATIONS	0	5 (0.27)	5 (0.08)
Haemoglobin decreased	0	5 (0.27)	5 (0.08)
NERVOUS SYSTEM DISORDERS	0	1 (0.05)	1 (0.02)
Dizziness	0	1 (0.05)	1 (0.02)
Somnolence	0	1 (0.05)	1 (0.02)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1 (0.02)	1 (0.05)	2 (0.03)
Angioedema	0	1 (0.05)	1 (0.02)
Dermatitis atopic	1 (0.02)	0	1 (0.02)
VASCULAR DISORDERS	0	1 (0.05)	1 (0.02)
Hypertensive urgency	0	1 (0.05)	1 (0.02)

The table only includes protocol-specified ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
Subjects are counted once within each system organ class or for each preferred term and may have had more than one AE.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 15MAR2021 (17:51)

by AESI Term	Number of Subjects with AE			Incidence Rate (Subjects with AE/100 Patient-Years)		
	Retacrit (N = 4496) n(%) [95% CI]	Silapo (N = 1841) n(%) [95% CI]	Total (N = 6337) n(%) [95% CI]	Retacrit Incidence per 100 patient-years [95% CI]	Silapo Incidence per 100 patient-years [95% CI]	Total Incidence per 100 patient-years [95% CI]
Adverse Events	199 (4.43) [3.8436, 5.0688]	242 (13.15) [11.6340, 14.7745]	441 (6.96) [6.3447, 7.6136]	2.3366 [2.0263, 2.6801]	8.1160 [7.1606, 9.1546]	3.8353 [3.4917, 4.2026]
Adverse Events of Special Interest	187 (4.16) [3.5945, 4.7845]	231 (12.55) [11.0678, 14.1477]	418 (6.60) [5.9972, 7.2354]	2.1949 [1.8943, 2.5287]	7.7244 [6.7925, 8.7399]	3.6315 [3.2972, 3.9895]
Pure Red Cell Aplasia	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0749]	0	0.0084 [0.0004, 0.0549]
Neutralising Antibodies	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0749]	0	0.0084 [0.0004, 0.0548]
Lack of Efficacy	12 (0.27) [0.1380, 0.4658]	22 (1.20) [0.7504, 1.8037]	34 (0.54) [0.3718, 0.7489]	0.1386 [0.0716, 0.2420]	0.6963 [0.4368, 1.0523]	0.2877 [0.1993, 0.4019]
Thromboembolic Events	176 (3.91) [3.3667, 4.5233]	213 (11.57) [10.1436, 13.1197]	389 (6.14) [5.5600, 6.7579]	2.0634 [1.7723, 2.3878]	7.0990 [6.2056, 8.0770]	3.3738 [3.0517, 3.7197]
ADR other than Events of Special Interest	12 (0.27) [0.1380, 0.4658]	16 (0.87) [0.4976, 1.4075]	28 (0.44) [0.2938, 0.6380]	0.1385 [0.0716, 0.2418]	0.5061 [0.2896, 0.8206]	0.2368 [0.1574, 0.3420]

The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
Confidence Interval is displayed in percentages.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.11 Date of Table Generation: 17AUG2020 (10:57)

	Number of Subjects with AE			Incidence Rate (Subjects with AE/100 Patient-Years)		
by AESI Term	Retacrit (N = 4496) n(%) [95% CI]	Silapo (N = 1841) n(%) [95% CI]	Total (N = 6337) n(%) [95% CI]	Retacrit Incidence per 100 patient-years [95% CI]	Silapo Incidence per 100 patient-years [95% CI]	Total Incidence per 100 patient-years [95% CI]
Adverse Events	199 (4.43) [3.8436, 5.0688]	240 (13.04) [11.5310, 14.6606]	439 (6.93) [6.3144, 7.5807]	2.3382 [2.0277, 2.6819]	8.0802 [7.1249, 9.1190]	3.8237 [3.4803, 4.1908]
Adverse Events of Special Interest	187 (4.16) [3.5945, 4.7845]	229 (12.44) [10.9649, 14.0336]	416 (6.56) [5.9671, 7.2025]	2.1964 [1.8956, 2.5305]	7.6871 [6.7557, 8.7027]	3.6196 [3.2856, 3.9774]
Pure Red Cell Aplasia	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0750]	0	0.0085 [0.0004, 0.0549]
Neutralising Antibodies	1 (0.02) [0.0012, 0.1443]	0	1 (0.02) [0.0008, 0.1024]	0.0115 [0.0006, 0.0750]	0	0.0085 [0.0004, 0.0549]
Lack of Efficacy	12 (0.27) [0.1380, 0.4658]	22 (1.20) [0.7504, 1.8037]	34 (0.54) [0.3718, 0.7489]	0.1387 [0.0717, 0.2422]	0.6992 [0.4387, 1.0568]	0.2882 [0.1997, 0.4025]
Thromboembolic Events	176 (3.91) [3.3667, 4.5233]	211 (11.46) [10.0411, 13.0052]	387 (6.11) [5.5298, 6.7249]	2.0649 [1.7736, 2.3895]	7.0594 [6.1668, 8.0372]	3.3616 [3.0398, 3.7072]
ADR other than Events of Special Interest	12 (0.27) [0.1380, 0.4658]	16 (0.87) [0.4976, 1.4075]	28 (0.44) [0.2938, 0.6380]	0.1386 [0.0716, 0.2420]	0.5083 [0.2908, 0.8241]	0.2372 [0.1577, 0.3426]

The table only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. Adverse Events: total of AESI and ADR.
Confidence Interval is displayed in percentages.
Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.
MedDRA v23 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 and Appendix 7.11 Date of Table Generation: 14SEP2020 (18:23)

The LIFETEST Procedure

Life Table Survival Estimates

Interval [Lower,	Upper)	Number Failed	Number Censored	Effective Sample Size	Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error	Evaluated at the Midpoint of the Interval PDF	PDF Standard Error	Hazard	Hazard Standard Error
0	2	0	401	6136.5	0	0	1.0000	0	0			0		0	
2	4	0	263	5804.5	0	0	1.0000	0	0			0		0	
4	6	0	301	5522.5	0	0	1.0000	0	0			0		0	
6	8	0	303	5220.5	0	0	1.0000	0	0			0		0	
8	10	1	241	4948.5	0.000202	0.000202	1.0000	0	0			0.000101	0.000101	0.000101	0.000101
10	12	0	281	4686.5	0	0	0.9998	0.000202	0.000202			0		0	
12	14	0	252	4420.0	0	0	0.9998	0.000202	0.000202			0		0	
14	16	0	271	4158.5	0	0	0.9998	0.000202	0.000202			0		0	
16	18	0	238	3904.0	0	0	0.9998	0.000202	0.000202			0		0	
18	20	0	254	3658.0	0	0	0.9998	0.000202	0.000202			0		0	
20	22	0	194	3434.0	0	0	0.9998	0.000202	0.000202			0		0	
22	24	0	214	3230.0	0	0	0.9998	0.000202	0.000202			0		0	
24	26	0	193	3026.5	0	0	0.9998	0.000202	0.000202			0		0	
26	28	0	133	2863.5	0	0	0.9998	0.000202	0.000202			0		0	
28	30	0	138	2728.0	0	0	0.9998	0.000202	0.000202			0		0	
30	32	0	132	2593.0	0	0	0.9998	0.000202	0.000202			0		0	
32	34	0	177	2438.5	0	0	0.9998	0.000202	0.000202			0		0	
34	36	0	1272	1714.0	0	0	0.9998	0.000202	0.000202			0		0	
36		0	1078	539.0	0	0	0.9998	0.000202	0.000202						

Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
6337	1	6336	99.98

The LIFETEST Procedure

Life Table Survival Estimates

Interval [Lower,	Upper)	Number Failed	Number Censored	Effective Sample Size	Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error	Evaluated at the Midpoint of the Interval PDF	PDF Standard Error	Hazard	Hazard Standard Error
0	2	0	401	6136.5	0	0	1.0000	0	0			0		0	
2	4	0	263	5804.5	0	0	1.0000	0	0			0		0	
4	6	0	301	5522.5	0	0	1.0000	0	0			0		0	
6	8	0	303	5220.5	0	0	1.0000	0	0			0		0	
8	10	0	241	4948.5	0	0	1.0000	0	0			0		0	
10	12	1	281	4687.5	0.000213	0.000213	1.0000	0	0			0.000107	0.000107	0.000107	0.000107
12	14	0	252	4420.0	0	0	0.9998	0.000213	0.000213			0		0	
14	16	0	271	4158.5	0	0	0.9998	0.000213	0.000213			0		0	
16	18	0	238	3904.0	0	0	0.9998	0.000213	0.000213			0		0	
18	20	0	254	3658.0	0	0	0.9998	0.000213	0.000213			0		0	
20	22	0	194	3434.0	0	0	0.9998	0.000213	0.000213			0		0	
22	24	0	214	3230.0	0	0	0.9998	0.000213	0.000213			0		0	
24	26	0	193	3026.5	0	0	0.9998	0.000213	0.000213			0		0	
26	28	0	133	2863.5	0	0	0.9998	0.000213	0.000213			0		0	
28	30	0	138	2728.0	0	0	0.9998	0.000213	0.000213			0		0	
30	32	0	132	2593.0	0	0	0.9998	0.000213	0.000213			0		0	
32	34	0	177	2438.5	0	0	0.9998	0.000213	0.000213			0		0	
34	36	0	1272	1714.0	0	0	0.9998	0.000213	0.000213			0		0	
36		0	1078	539.0	0	0	0.9998	0.000213	0.000213						

Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
6337	1	6336	99.98

The LIFETEST Procedure

Life Table Survival Estimates

Interval [Lower,	Upper)	Number Failed	Number Censored	Effective Sample Size	Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error	Evaluated at the Midpoint of the Interval PDF	PDF Standard Error	Hazard	Hazard Standard Error
0	2	10	398	6138.0	0.00163	0.000515	1.0000	0	0			0.000815	0.000257	0.000815	0.000258
2	4	6	258	5800.0	0.00103	0.000422	0.9984	0.00163	0.000515			0.000516	0.000211	0.000518	0.000211
4	6	3	297	5516.5	0.000544	0.000314	0.9973	0.00266	0.000665			0.000271	0.000157	0.000272	0.000157
6	8	0	303	5213.5	0	0	0.9968	0.00320	0.000735			0		0	
8	10	1	241	4941.5	0.000202	0.000202	0.9968	0.00320	0.000735			0.000101	0.000101	0.000101	0.000101
10	12	1	281	4679.5	0.000214	0.000214	0.9966	0.00341	0.000762			0.000106	0.000106	0.000107	0.000107
12	14	1	252	4412.0	0.000227	0.000227	0.9964	0.00362	0.000791			0.000113	0.000113	0.000113	0.000113
14	16	2	269	4150.5	0.000482	0.000341	0.9962	0.00384	0.000822			0.000240	0.000170	0.000241	0.00017
16	18	3	235	3896.5	0.000770	0.000444	0.9957	0.00432	0.000889			0.000383	0.000221	0.000385	0.000222
18	20	2	252	3650.0	0.000548	0.000387	0.9949	0.00509	0.000992			0.000273	0.000193	0.000274	0.000194
20	22	0	193	3425.5	0	0	0.9944	0.00564	0.00106			0		0	
22	24	4	211	3223.5	0.00124	0.000620	0.9944	0.00564	0.00106			0.000617	0.000308	0.000621	0.00031
24	26	0	191	3018.5	0	0	0.9931	0.00687	0.00123			0		0	
26	28	0	132	2857.0	0	0	0.9931	0.00687	0.00123			0		0	
28	30	0	137	2722.5	0	0	0.9931	0.00687	0.00123			0		0	
30	32	0	131	2588.5	0	0	0.9931	0.00687	0.00123			0		0	
32	34	1	177	2434.5	0.000411	0.000411	0.9931	0.00687	0.00123			0.000204	0.000204	0.000205	0.000205
34	36	0	1269	1710.5	0	0	0.9927	0.00728	0.00129			0		0	
36		0	1076	538.0	0	0	0.9927	0.00728	0.00129						

Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
6337	34	6303	99.46

The LIFETEST Procedure

Life Table Survival Estimates

Interval [Lower,	Upper)	Number Failed	Number Censored	Effective Sample Size	Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error	Evaluated at the Midpoint of the Interval PDF	PDF Standard Error	Hazard	Hazard Standard Error
0	2	55	388	6143.0	0.00895	0.00120	1.0000	0	0			0.00448	0.000601	0.004497	0.000606
2	4	43	248	5770.0	0.00745	0.00113	0.9910	0.00895	0.00120			0.00369	0.000561	0.00374	0.00057
4	6	32	280	5463.0	0.00586	0.00103	0.9837	0.0163	0.00164			0.00288	0.000508	0.002937	0.000519
6	8	33	282	5150.0	0.00641	0.00111	0.9779	0.0221	0.00192			0.00313	0.000544	0.003214	0.00056
8	10	25	226	4863.0	0.00514	0.00103	0.9716	0.0284	0.00219			0.00250	0.000498	0.002577	0.000515
10	12	23	266	4592.0	0.00501	0.00104	0.9666	0.0334	0.00240			0.00242	0.000504	0.002511	0.000524
12	14	26	241	4315.5	0.00602	0.00118	0.9618	0.0382	0.00259			0.00290	0.000567	0.003021	0.000593
14	16	19	249	4044.5	0.00470	0.00108	0.9560	0.0440	0.00281			0.00225	0.000514	0.002354	0.00054
16	18	18	224	3789.0	0.00475	0.00112	0.9515	0.0485	0.00298			0.00226	0.000531	0.002381	0.000561
18	20	15	232	3543.0	0.00423	0.00109	0.9470	0.0530	0.00315			0.00200	0.000517	0.002121	0.000548
20	22	23	169	3327.5	0.00691	0.00144	0.9430	0.0570	0.00331			0.00326	0.000677	0.003468	0.000723
22	24	15	207	3116.5	0.00481	0.00124	0.9365	0.0635	0.00355			0.00225	0.000581	0.002412	0.000623
24	26	12	170	2913.0	0.00412	0.00119	0.9320	0.0680	0.00372			0.00192	0.000553	0.002064	0.000596
26	28	11	120	2756.0	0.00399	0.00120	0.9281	0.0719	0.00387			0.00185	0.000557	0.002	0.000603
28	30	15	123	2623.5	0.00572	0.00147	0.9244	0.0756	0.00401			0.00264	0.000680	0.002867	0.00074
30	32	10	118	2488.0	0.00402	0.00127	0.9191	0.0809	0.00421			0.00185	0.000583	0.002014	0.000637
32	34	9	152	2343.0	0.00384	0.00128	0.9154	0.0846	0.00435			0.00176	0.000585	0.001924	0.000641
34	36	2	1219	1648.5	0.00121	0.000857	0.9119	0.0881	0.00449			0.000553	0.000391	0.000607	0.000429
36		3	1034	520.0	0.00577	0.00332	0.9108	0.0892	0.00455						

Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
6337	389	5948	93.86

The LIFETEST Procedure

Life Table Survival Estimates

Interval [Lower,	Upper)	Number Failed	Number Censored	Effective Sample Size	Conditional Probability of Failure	Conditional Probability Standard Error	Survival	Failure	Survival Standard Error	Median Residual Lifetime	Median Standard Error	Evaluated at the Midpoint of the Interval PDF	PDF Standard Error	Hazard	Hazard Standard Error
0	2	17	394	6140.0	0.00277	0.000671	1.0000	0	0			0.00138	0.000335	0.001386	0.000336
2	4	2	262	5795.0	0.000345	0.000244	0.9972	0.00277	0.000671			0.000172	0.000122	0.000173	0.000122
4	6	2	295	5514.5	0.000363	0.000256	0.9969	0.00311	0.000713			0.000181	0.000128	0.000181	0.000128
6	8	0	302	5214.0	0	0	0.9965	0.00347	0.000757			0		0	
8	10	1	239	4943.5	0.000202	0.000202	0.9965	0.00347	0.000757			0.000101	0.000101	0.000101	0.000101
10	12	1	282	4682.0	0.000214	0.000214	0.9963	0.00368	0.000784			0.000106	0.000106	0.000107	0.000107
12	14	0	250	4415.0	0	0	0.9961	0.00389	0.000812			0		0	
14	16	0	270	4155.0	0	0	0.9961	0.00389	0.000812			0		0	
16	18	2	237	3901.5	0.000513	0.000362	0.9961	0.00389	0.000812			0.000255	0.000180	0.000256	0.000181
18	20	0	253	3654.5	0	0	0.9956	0.00440	0.000888			0		0	
20	22	0	194	3431.0	0	0	0.9956	0.00440	0.000888			0		0	
22	24	2	212	3228.0	0.000620	0.000438	0.9956	0.00440	0.000888			0.000308	0.000218	0.00031	0.000219
24	26	0	191	3024.5	0	0	0.9950	0.00502	0.000989			0		0	
26	28	0	133	2862.5	0	0	0.9950	0.00502	0.000989			0		0	
28	30	1	137	2727.5	0.000367	0.000367	0.9950	0.00502	0.000989			0.000182	0.000182	0.000183	0.000183
30	32	0	131	2592.5	0	0	0.9946	0.00538	0.00105			0		0	
32	34	0	177	2438.5	0	0	0.9946	0.00538	0.00105			0		0	
34	36	0	1272	1714.0	0	0	0.9946	0.00538	0.00105			0		0	
36		0	1078	539.0	0	0	0.9946	0.00538	0.00105						

Summary of the Number of Censored and Uncensored Values

Total	Failed	Censored	Percent Censored
6337	28	6309	99.56

Two cases (1985966 and 1244227) that were reported in the Clinical Database as Adverse Drug Reactions (ADRs) were not ADRs as both events were assessed as unrelated to the suspect drug epoetin zeta by both the Investigator and the Company. The CIOMs reports for these two cases will not be provided in the CSR.

Bg-001-0024/68/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 25JUN2014 (140) E:	AESI	S: Yes C: 1 D: 25JUN2014	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 15OCT2016 (440) E:	AESI	S: Yes C: 1, 3 D: 17OCT2016	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-004-0004/75/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC BRAIN STROKE	S: 25MAY2014 (185) E: 25MAY2014 (185)	AESI	S: Yes C: 1 D: 25MAY2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-004-0041/76/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 30JUL2016 (662) E: 06AUG2016 (669)	AESI	S: Yes C: 1, 3 D: 06AUG2016	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-004-0094/81/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 08NOV2018 (812) E:	AESI	S: Yes C: 1, 2, 3 D: 18NOV2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-006-0039/66/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ BRAIN'S STROKE	S: JUN2017 E:	AESI	S: Yes C: 1, 2, 3 D: JUN2017	FATAL		POST-THERAPY	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-014-0002/80/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: E:	AESI	S: Yes C: 1 D: 12DEC2013	FATAL	NOT APPLICABLE		NOT RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY THROMBOEMBOLISM	S: E:	AESI	S: Yes C: 1 D: 12DEC2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-014-0003/51/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 09APR2015 (534)	AESI	S: Yes C: 1 D: 09APR2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-014-0004/84/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC BRAIN STROKE	S: 24APR2014 (184) E: 24APR2014 (184)	AESI	S: Yes C: 1, 2 D: 24APR2014	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-015-0017/62/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ LEFT HEMISPHERIC STROKE	S: 01OCT2015 (199) E: 01OCT2015 (199)	AESI	S: Yes C: 1, 2 D: 01OCT2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-025-0011/72/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26OCT2017 (497) E:	AESI	S: Yes C: 1, 2, 3 D: 27OCT2017	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Cr-005-0002/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01MAR2017 (891) E:	AESI	S: Yes C: 1, 2, 3 D: 06MAR2017	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Cr-005-0014/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Subdural haematoma/ HEAD TRAUMA DUE TO DOWNFALL, SUBDURAL HEMATOMA, OEDEMA CEREBRI, COMA CEREBRI	S: 09MAY2016 (363) E:	AESI	S: Yes C: 1, 3 D: 11MAY2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Es-024-0025/87/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 21APR2015 (777)	AESI	S: Yes C: 1 D: 21APR2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Es-024-0038/86/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 30AUG2017 (317) E:	AESI	S: Yes C: 1, 2, 3 D: 30AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Fin-001-0002/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11DEC2015 (971) E: 16DEC2015 (976)	AESI	S: Yes C: 1, 2, 3 D: 16DEC2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE ACCIDENT	S: 08APR2013 (112) E: 10APR2013 (114)	AESI	S: Yes C: 1, 2 D: 10APR2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-012-0007/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 06APR2011 (153) E: 07APR2011 (154)	AESI	S: Yes C: 1, 2, 3 D: 07APR2011	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-012-0017/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXIA	S: 30JAN2013 (665) E: 30JAN2013 (665)	AESI	S: Yes C: 1, 2, 3 D: 30JAN2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-012-0022/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Product issues/ Thrombosis in device/ THROMBOSIS CENTRAL VENOUS CATHETER	S: 26SEP2012 (484) E: 16NOV2012 (535)	AESI	S: Yes C: 1, 2, 3 D: 16NOV2012	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-027-0028/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 28AUG2013 (636) E: 03SEP2013 (642)	AESI	S: Yes C: 1, 2, 3 D: 03SEP2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-048-0041/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: E:	AESI	S: Yes C: 1 D: 18APR2018	FATAL	UNKNOWN		NO DATA
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: E:	AESI	S: Yes C: 1 D: 18APR2018	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-069-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Infarction/ SECOND INFARCT	S: 18OCT2018 (1479) E:	AESI	S: Yes C: 1, 6 D: 18OCT2018	FATAL		POST-THERAPY	NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-083-0006/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 24JUL2014 (1002) E: 26JUL2014 (1004)	AESI	S: Yes C: 1 D: 26JUL2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-083-0008/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: E: 22MAY2014 (898)	AESI	S: Yes C: 1, 2, 3 D: 22MAY2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-093-0085/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ MIDDLE LEFT CEREBRAL ARTERY INFARCTION	S: 11MAY2014 (47) E: 12MAY2014 (48)	AESI	S: Yes C: 1, 2, 3 D: 12MAY2014	FATAL	UNKNOWN		N/A
Nervous system disorders/ Cerebral ischaemia/ RESPIRATORY INSUFFICIENCY DUE TO LEFTSIDE BRAIN ISCHEMIA	S: 11MAY2014 (47) E: 12MAY2014 (48)	AESI	S: Yes C: 1, 2, 3 D: 12MAY2014	FATAL	UNKNOWN		N/A

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-094-0032/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ SUSPECTED OF HEART ATTACK	S: 22SEP2017 (740) E:	AESI	S: Yes C: 1 D: 22SEP2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ SUSPECTED ACUTE MYOCARDIAL INFARCTION	S: 13FEB2015 (439) E: 13FEB2015 (439)	AESI	S: Yes C: 1, 2, 3 D: 13FEB2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-115-0015/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial thrombosis/ ARTERIAL THROMBOSIS	S: 14MAR2011 (22) E: 22MAR2011 (30)	AESI	S: Yes C: 1 D: 22MAR2011	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 29DEC2013 (910) E: 29DEC2013 (910)	AESI	S: Yes C: 1, 2 D: 29DEC2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-152-0025/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 09OCT2015 (621)	AESI	S: Yes C: 1 D: 09OCT2015	FATAL		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01MAY2014 (318) E: 11MAY2014 (328)	AESI	S: Yes C: 1 D: 11MAY2014	FATAL		NO DATA	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-463-0008/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Basal ganglia haemorrhage/ BASAL GANGLIA HEMORRHAGE RIGHT	S: E: 01JUL2014 (488)	AESI	S: Yes C: 1, 2 D: 01JUL2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED
Injury, poisoning and procedural complications/ Subdural haematoma/ SUBDURAL HEMATOMA RIGHT	S: E: 01JUL2014 (488)	AESI	S: Yes C: 1, 2 D: 01JUL2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06DEC2013 (102) E:	AESI	S: Yes C: 1 D: 06DEC2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY ARTERY EMBOLISM	S: 01SEP2014 (97) E: 09DEC2014 (196)	AESI	S: Yes C: 1 D: 09DEC2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-471-0016/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: E:	AESI	S: Yes C: 1, 2 D: 19SEP2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Ge-471-0033/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ DECOMPENSATION CHRONIC RIGHT HEART FAILURE AND HEART ATTACK	S: 08DEC2016 (731) E:	AESI	S: Yes C: 1 D: 08DEC2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 29OCT2014 (164) E: 31OCT2014 (166)	AESI	S: Yes C: 1, 2 D: 31OCT2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22FEB2015 (256) E: 26FEB2015 (260)	AESI	S: Yes C: 1, 2, 3 D: 26FEB2015	FATAL		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 18MAR2014 (297) E: 18MAR2014 (297)	AESI	S: Yes C: 1, 2 D: 18MAR2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-013-0002/67/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE CORONARY INFARCTION	S: 05JUL2015 (754) E: 05JUL2015 (754)	AESI	S: Yes C: 1 D: 05JUL2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21AUG2013 (149) E: 21AUG2013 (149)	AESI	S: Yes C: 1, 2, 3 D: 21AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-034-0009/73/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 05APR2016 (407) E:	AESI	S: Yes C: 1, 2 D: 05APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-034-0010/78/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ VASCULAR STROKE	S: 14OCT2015 (233) E:	AESI	S: Yes C: 1, 2 D: 14OCT2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: E: 14JAN2015 (178)	AESI	S: Yes C: 1, 3 D: 14JAN2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: AUG2017 E:	AESI	S: Yes C: 1 D: 20AUG2017	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 30AUG2013 (99) E: 30AUG2013 (99)	AESI	S: Yes C: 1, 2, 3 D: 30AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: 03JUN2014 (288) E:	AESI	S: Yes C: 1, 6 D: 03JUL2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20OCT2013 (7) E:	AESI	S: Yes C: 1 D: 29OCT2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 07JUL2016 (144) E:	AESI	S: Yes C: 1 D: 07JUL2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24NOV2016 (231) E:	AESI	S: Yes C: 1, 2, 3 D: 24NOV2016	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 24JUL2015 (523) E: 31JUL2015 (530)	AESI	S: Yes C: 1, 2, 3 D: 31JUL2015	FATAL	DOSE REDUCED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-052-0010/79/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 30DEC2015 (658) E: 01JAN2016 (660)	AESI	S: Yes C: 1 D: 01JAN2016	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-059-0006/46/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART INFARCTION	S: 10FEB2017 (122) E:	AESI	S: Yes C: 1 D: 10FEB2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-062-0006/79/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 05NOV2015 (43) E: 05NOV2015 (43)	AESI	S: Yes C: 1 D: 05NOV2015	FATAL	NOT APPLICABLE		N/A

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Gr-065-0005/86/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CORONARY INFARCTION	S: E:	AESI	S: Yes C: 1 D: 29OCT2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

It-038-0014/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Haemorrhagic stroke/ HAEMORRHAGIC ICTUS	S: 09AUG2012 (7) E: 11AUG2012 (9)	AESI	S: Yes C: 1, 2, 3 D: 11AUG2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: E: 07APR2014 (67)	AESI	S: Yes C: 1 D: 07APR2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

It-093-0005/77/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 02SEP2013 (186) E:	AESI	S: Yes C: 1 D: 02SEP2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

It-116-0018/81/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 19MAR2016 (858) E:	AESI	S: Yes C: 1 D: 19MAR2016	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

It-116-0021/70/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: E: 13NOV2014 (352)	AESI	S: Yes C: 1 D: 13NOV2014	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular disorder/ CEREBROVASCULAR EVENT	S: 20MAR2014 (15) E:	AESI	S: Yes C: 1 D: 20MAR2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

It-120-0019/83/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ CEREBRAL STROKE	S: 04NOV2014 (114) E: 15DEC2014 (155)	AESI	S: Yes C: 1, 2, 3 D: 15DEC2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 26AUG2017 (970) E: 26AUG2017 (970)	AESI	S: Yes C: 1 D: 30AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 09JAN2014 (697) E: 11JAN2014 (699)	AESI	S: Yes C: 1, 2, 3 D: 11JAN2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Sw-005-0014/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22NOV2013 (648) E: 24NOV2013 (650)	AESI	S: Yes C: 1, 2 D: 24NOV2013	FATAL	NOT APPLICABLE		NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE INFARCTION	S: 26APR2016 (610) E:	AESI	S: Yes C: 1 D: 26APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Sw-011-0023/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CARDIAC INFACTION	S: 03JUN2016 (932) E: 07JUN2016 (936)	AESI	S: Yes C: 1, 2, 3 D: 07JUN2016	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Sw-011-0028/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	S: Yes C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	NO DATA
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	S: Yes C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	S: Yes C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Sw-018-0003/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20DEC2012 (16) E: 20DEC2012 (16)	AESI	S: Yes C: 1, 3 D: 20DEC2012	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Sw-018-0008/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01JUN2015 (757) E: 07JUN2015 (763)	AESI	S: Yes C: 1, 2 D: 07JUN2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 03SEP2012 (596) E:	AESI	S: Yes C: 1, 3, 7 D: 03SEP2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 09DEC2011 (324) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 09DEC2011	FATAL	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ MEDULLA OBLONGATA BLEEDING	S: 13MAR2011 (55) E:	AESI	S: Yes C: 1, 3, 7 D: 13MAR2011	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 14OCT2012 (608) E:	AESI	S: Yes C: 1, 3, 7 D: 14OCT2012	FATAL	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01JUL2014 (411) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 01JUL2014	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism arterial/ THROMBOEMBOLIC OCCLUSION OF FEMORAL ARTERY WITH CRITICAL ISCHAEMIA OF LEFT LEG.	S: 21SEP2018 (185) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 21SEP2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 13OCT2013 (461) E:	AESI	S: Yes C: 1, 3, 7 D: 13OCT2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 11NOV2014 (818) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 11NOV2014	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 15OCT2017 (964) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 15OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

De-008-B059/C/F
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 14NOV2012 (134) E:	AESI	S: Yes C: 1, 7 D: 14NOV2012	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 16DEC2013 (1063) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 17DEC2013	FATAL	NOT APPLICABLE		UNLIKELY RELATED
Gastrointestinal disorders/ Mesenteric vein thrombosis/ MESENTERIC THROMBOSIS	S: 17DEC2013 (1064) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 17DEC2013	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 23AUG2011 (214) E:	AESI	S: Yes C: 1, 3, 7 D: 23AUG2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	S: Yes C: 1, 7 D: 01APR2011	FATAL	DRUG WITHDRAWN		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	S: Yes C: 1, 7 D: 01APR2011	FATAL	UNKNOWN		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	S: Yes C: 1, 7 D: 01APR2011	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 16SEP2011 (115) E:	AESI	S: Yes C: 1, 7 D: 16SEP2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26DEC2011 (120) E:	AESI	S: Yes C: 1, 7 D: 26DEC2011	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01SEP2011 (197) E:	AESI	S: Yes C: 1, 7 D: 01SEP2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05MAY2012 (443) E:	AESI	S: Yes C: 1, 7 D: 05MAY2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 17JUN2014 (1052) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 17JUN2014	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05JUL2012 (448) E:	AESI	S: Yes C: 1, 3, 7 D: 05JUL2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24MAY2019 (288) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 24MAY2019	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE OF HIS LEGS	S: 07JAN2014 (1001) E: 25JAN2014 (1019)	AESI	S: Yes C: 1, 3, 7 D: 25JAN2014	FATAL	DRUG WITHDRAWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 16APR2012 (18) E:	AESI	S: Yes C: 1, 3, 5, 7 D: 13JAN2014	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04JUL2016 (301) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 04JUL2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18JUL2012 (154) E:	AESI	S: Yes C: 1, 7 D: 18JUL2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01FEB2014 (913) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 01FEB2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 01JUL2012 (308) E:	AESI	S: Yes C: 1, 7 D: 01JUL2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18MAR2013 (567) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 18MAR2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

De-048-B006/C/M
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04DEC2012 (156) E: 10DEC2012 (162)	AESI	S: Yes C: 1, 3, 7 D: 10DEC2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

De-048-B008/C/M
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 13AUG2013 (587) E:	AESI	S: Yes C: 1, 3, 7 D: 13AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Venous occlusion/ VENOUS OCCLUSION OF ARTERIA BRACHIALIS LEFT	S: 03JAN2014 (563) E:	AESI	S: Yes C: 1, 3, 7 D: 03JAN2014	FATAL	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 07MAY2012 (165) E: 23MAY2012 (181)	AESI	S: Yes C: 1, 2, 3, 7 D: 23SEP2014	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 23SEP2014 (1034) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 23SEP2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 16DEC2012 (273) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 16DEC2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04JUL2015 (788) E:	AESI	S: Yes C: 1, 7 D: 04JUL2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 17OCT2016 (358) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 17OCT2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Infections and infestations/ Gangrene/ GANGRENE OF TOES	S: 13DEC2017 (43) E:	ADR	S: Yes C: 1, 2, 3, 7 D: 13DEC2017	FATAL	NOT APPLICABLE		POSSIBLE RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PROGRESSION OF PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 13DEC2017 (43) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 13DEC2017	FATAL	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 07APR2016 (143) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 07APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral embolism/ ARTERIAL EMBOLISM OF RIGHT FOOT	S: 18AUG2018 (1001) E:	AESI	S: Yes C: 1, 3, 7 D: 18AUG2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 23JUL2015 (207) E:	AESI	S: Yes C: 1, 2, 7 D: 23JUL2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11FEB2016 (116) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 11FEB2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ PROGRESSIVE ARTERIAL OCCLUSIVE DISEASE	S: 10AUG2017 (686) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 10AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

De-067-B005/C/M
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 02JUN2015 (495) E:	AESI	S: Yes C: 1, 2, 7 D: 02JUN2015	FATAL	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 24AUG2015 (215) E:	AESI	S: Yes C: 1, 3, 7 D: 24AUG2015	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 09DEC2016 (562) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 09DEC2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21JUN2015 (69) E:	AESI	S: Yes C: 1, 2, 7 D: 21JUN2015	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21SEP2015 (197) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 21SEP2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 30MAY2016 (238) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 30MAY2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 20JUL2017 (535) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 20JUL2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 12MAY2018 (831) E:	AESI	S: Yes C: 1, 2, 7 D: 12MAY2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 12MAY2017 (563) E: 12MAY2017 (563)	AESI	S: Yes C: 1, 3, 7 D: 12MAY2017	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE FONTAINE STAGE IV	S: 17OCT2017 (545) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 17OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 12JUN2018 (782) E:	AESI	S: Yes C: 1, 2, 7 D: 12JUN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 14AUG2017 (607) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 14AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 16OCT2017 (674) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 16OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06JAN2018 (723) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 06JAN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26JUN2018 (921) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 26JUN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 13MAR2016 (96) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 13MAR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HEMORRHAGE	S: 04NOV2016 (332) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 04NOV2016	FATAL	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 29SEP2017 (660) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 29SEP2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21DEC2018 (1059) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 21DEC2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE STAGE IV	S: 12MAR2018 (777) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 12MAR2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 25APR2018 (821) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 25APR2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 06NOV2017 (669) E:	AESI	S: Yes C: 1, 3, 7 D: 06NOV2017	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Investigations/ Haemoglobin decreased/ HEMOGLOBIN DECREASE	S: 05MAR2016 (54) E:	ADR	S: Yes C: 1, 2, 7 D: 09MAR2016	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 14JUL2016 (21) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 14JUL2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 13JAN2017 (61) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 13JAN2017	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Carotid artery restenosis/ CAROTIS STENOSIS	S: 26SEP2018 (857) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 26SEP2018	FATAL	NOT APPLICABLE		UNLIKELY RELATED
Nervous system disorders/ Ischaemic stroke/ LEFT HEMISPHERIC ISCHEMIA AT CAROTIS STENOSIS	S: 26SEP2018 (857) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 26SEP2018	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: APR2017 E:	AESI	S: Yes C: 1, 2, 3, 7 D: 18APR2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 06SEP2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 06SEP2017	FATAL	UNKNOWN		UNKNOWN
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 06SEP2017	FATAL	UNKNOWN		UNKNOWN

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 09FEB2020 (956) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 09FEB2020	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26OCT2017 (256) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 26OCT2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ UNSPECIFIED STROKE	S: 07APR2019 (187) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 07APR2019	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11MAR2019 (438) E:	AESI	S: Yes C: 1, 2, 7 D: 11MAR2019	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20NOV2017 (223) E:	AESI	S: Yes C: 1, 2, 3, 7 D: 20NOV2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	S: SAE C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS FEMORAL	S: 25APR2019 (127) E:	AESI	S: Yes C: 1, 3, 7 D: 25APR2019	UNKNOWN	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes deaths due to protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:36)

Bg-001-0024/68/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 25JUN2014 (140) E:	AESI	C: 1 D: 25JUN2014	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 15OCT2016 (440) E:	AESI	C: 1, 3 D: 17OCT2016	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-004-0004/75/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC BRAIN STROKE	S: 25MAY2014 (185) E: 25MAY2014 (185)	AESI	C: 1 D: 25MAY2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-004-0017/68/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral artery thrombosis/ THROMBOSIS OF RIGHT ILEAC ARTERY	S: 01MAR2015 (399) E: 24MAR2015 (422)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ NONTRANSMURAL MYOCARDIAL INFARCTION	S: 24MAR2015 (394) E:	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENT	S: 09MAY2015 (440) E:	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC BRAIN STROKE	S: 23SEP2016 (760) E: 27SEP2016 (764)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-004-0041/76/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 30JUL2016 (662) E: 06AUG2016 (669)	AESI	C: 1, 3 D: 06AUG2016	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 08NOV2018 (812) E:	AESI	C: 1, 2, 3 D: 18NOV2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE BLSMA	S: 17MAR2018 (549) E: 03APR2018 (566)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-006-0039/66/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ BRAIN'S STROKE	S: JUN2017 E:	AESI	C: 1, 2, 3 D: JUN2017	FATAL		POST-THERAPY	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-014-0002/80/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: E:	AESI	C: 1 D: 12DEC2013	FATAL	NOT APPLICABLE		NOT RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY THROMBOEMBOLISM	S: E:	AESI	C: 1 D: 12DEC2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 09APR2015 (534)	AESI	C: 1 D: 09APR2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC BRAIN STROKE	S: 24APR2014 (184) E: 24APR2014 (184)	AESI	C: 1, 2 D: 24APR2014	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-014-0025/57/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ THROMBOSISA. TIBIALISVEIN	S: 16MAR2016 (43) E:	AESI	C: 2, 3 D: 24APR2016	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-014-0026/33/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Venous thrombosis/ LEFT FEMUROPOPLITEAL PHLEBOTHROMBOSIS	S: E:	AESI	C: 2, 3 D: 27FEB2016	UNKNOWN	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-015-0017/62/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ LEFT HEMISPHERIC STROKE	S: 01OCT2015 (199) E: 01OCT2015 (199)	AESI	C: 1, 2 D: 01OCT2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-025-0011/72/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26OCT2017 (497) E:	AESI	C: 1, 2, 3 D: 27OCT2017	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Bg-025-0014/84/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 08AUG2017 (335) E: 11DEC2017 (460)	AESI	C: 2, 3, 6 D: 28DEC2017	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 05MAY2017 (956) E: 12MAY2017 (963)	AESI	C: 2, 3, 5, 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01MAR2017 (891) E:	AESI	C: 1, 2, 3 D: 06MAR2017	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ CEREBROVASCULAR INSULT	S: 01FEB2017 (828) E: 25FEB2017 (852)	AESI	C: 3 D: 03APR2017	RECOVERED/ RESOLVED WITH SEQUELAE		POST-THERAPY	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Cr-005-0014/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Subdural haematoma/ HEAD TRAUMA DUE TO DOWNFALL, SUBDURAL HEMATOMA, OEDEMA CEREBRI, COMA CEREBRI	S: 09MAY2016 (363) E:	AESI	C: 1, 3 D: 11MAY2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 10DEC2015 (49) E:	AESI	C: 2, 3 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D: 18OCT2016	UNKNOWN	UNKNOWN		RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 02NOV2015 (6) E: 10NOV2015 (14)	AESI	C: 3 D: 18OCT2016	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ CVI	S: 26OCT2017 (714) E: 16NOV2017 (735)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Thrombosis/ THROMBOSIS	S: 03MAY2017 (150) E:	AESI	C: 3, 6 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 21APR2015 (777)	AESI	C: 1 D: 21APR2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 30AUG2017 (317) E:	AESI	C: 1, 2, 3 D: 30AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ ACVA	S: 06JUN2013 (261) E: 03JUL2013 (288)	AESI	C: 3 D: 27JAN2014	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Arteriovenous fistula thrombosis/ THROMBOSIS NATIVE ARTERIOVENOUS FISTULA	S: 13OCT2018 (876) E:	AESI	C: 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Arteriovenous fistula thrombosis/ THROMBOSIS NATIVE ARTERIOVENOUS FISTULA	S: 16FEB2019 (853) E:	AESI	C: 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: FEB2017 E: FEB2017	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary thrombosis/ THROMBOSIS PULMONAR BILATERAL	S: 10FEB2017 (201) E: 20FEB2017 (211)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11DEC2015 (971) E: 16DEC2015 (976)	AESI	C: 1, 2, 3 D: 16DEC2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Fin-001-0005/57/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 08NOV2016 (469) E:	AESI	C: 3 D:	UNKNOWN		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 27SEP2015 (685) E: 30SEP2015 (688)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 23OCT2015 (711) E: 26OCT2015 (714)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 28APR2014 (48) E:	AESI	C: 2, 3 D: 19APR2015	RECOVERED/ RESOLVED	DOSE NOT CHANGED		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ AMI	S: 11MAY2012 (68) E:	AESI	C: 2, 3 D: 25NOV2013	RECOVERED/ RESOLVED		NO DATA	NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 14JUL2013 (497) E:	AESI	C: 2, 3 D: 25NOV2013	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Fr-064-0019/92/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE ACCIDENT	S: 08APR2013 (112) E: 10APR2013 (114)	AESI	C: 1, 2 D: 10APR2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0007/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 06APR2011 (153) E: 07APR2011 (154)	AESI	C: 1, 2, 3 D: 07APR2011	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0017/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXIA	S: 30JAN2013 (665) E: 30JAN2013 (665)	AESI	C: 1, 2, 3 D: 30JAN2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0022/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Product issues/ Thrombosis in device/ THROMBOSIS CENTRAL VENOUS CATHETER	S: 26SEP2012 (484) E: 16NOV2012 (535)	AESI	C: 1, 2, 3 D: 16NOV2012	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0070/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NON STEMI	S: 08APR2017 (410) E: 12APR2017 (414)	AESI	C: 2, 3 D: 06JUL2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0071/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 26JUL2017 (534) E: 17AUG2017 (556)	AESI	C: 3 D:	RECOVERED/ RESOLVED		POST-THERAPY	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0075/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 10NOV2016 (207) E: 15NOV2016 (212)	AESI	C: 2, 3 D: 12OCT2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PAVK	S: 10JAN2017 (268) E: 10JAN2017 (268)	AESI	C: 6 D: 12OCT2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-012-0080/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 19NOV2017 (308) E: 27NOV2017 (316)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-027-0010/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEX	S: 03FEB2012 (343) E: 17FEB2012 (357)	AESI	C: 3 D:	RECOVERED/ RESOLVED		NO DATA	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-027-0024/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 28JUL2012 (363) E: 16AUG2012 (382)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-027-0028/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 28AUG2013 (636) E: 03SEP2013 (642)	AESI	C: 1, 2, 3 D: 03SEP2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-046-0005/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CARDIAC INFARCTION	S: 11SEP2013 (660) E:	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-046-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 15AUG2012 (268) E: 15AUG2012 (268)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-048-0014/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: E:	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-048-0037/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Basal ganglia haemorrhage/ BASAL GANGLIA HAEMORRHAGE	S: 25MAR2015 (70) E: 04APR2015 (80)	AESI	C: 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Pelvic venous thrombosis/ PELVIC VEIN THROMBOSIS	S: 10OCT2016 (533) E:	AESI	C: 3 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-048-0041/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: E:	AESI	C: 1 D: 18APR2018	FATAL	UNKNOWN		NO DATA
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: E:	AESI	C: 1 D: 18APR2018	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-069-0009/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ INFARCT ON THE RIGHT BRAIN SIDE	S: 23OCT2015 (404) E:	AESI	C: 6 D: 17JAN2016	UNKNOWN	NOT APPLICABLE		N/A
Nervous system disorders/ Cerebral infarction/ INFARCT ON THE RIGHT BRAIN SIDE	S: 23OCT2015 (404) E:	AESI	C: 6 D: 17JAN2016	UNKNOWN	NOT APPLICABLE		NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-069-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 13MAR2015 (164) E:	AESI	C: 3 D: 18OCT2018	UNKNOWN	UNKNOWN		RELATED
Vascular disorders/ Infarction/ SECOND INFARCT	S: 18OCT2018 (1479) E:	AESI	C: 1, 6 D: 18OCT2018	FATAL		POST-THERAPY	NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-083-0006/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Infarction/ POSTINFARCT	S: E:	AESI	C: 6 D: 26JUL2014	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 24JUL2014 (1002) E: 26JUL2014 (1004)	AESI	C: 1 D: 26JUL2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-083-0008/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: E: 22MAY2014 (898)	AESI	C: 1, 2, 3 D: 22MAY2014	FATAL	NOT APPLICABLE		NOT RELATED
Vascular disorders/ Thrombosis/ LOWER LEG THROMBOSIS	S: 01NOV2013 (696) E:	AESI	C: 2, 3 D: 22MAY2014	UNKNOWN	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0020/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Diarrhoea/ DIARRHEA	S: E: 02APR2012 (35)	ADR	C: 3 D:	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0045/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 20FEB2016 (965) E: 23FEB2016 (968)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0056/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 04APR2015 (580) E: 10APR2015 (586)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0057/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS	S: 08OCT2013 (56) E: 15OCT2013 (63)	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 08OCT2013 (56) E: 15OCT2013 (63)	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0076/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI DUE TO ACUTE, PROXIMAL OCCLUSION OF THE RCX	S: 02JUL2015 (517) E: 07JUL2015 (522)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0079/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Thrombosis/ THROMBOSIS OF V. FIBULARIS (RIGHT SIDE)	S: 16MAR2015 (368) E: 20MAR2015 (372)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		RELATED
Vascular disorders/ Thrombosis/ THROMBOSIS OF V. FIBULARIS POSTERIOR (RIGHT SIDE)	S: 11AUG2015 (516) E: 21AUG2015 (526)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ MIDDLE CEREBRAL ARTERY INFARCTION	S: 25JUN2016 (823) E:	AESI	C: 3, 5 D: 04OCT2016	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0085/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ MIDDLE LEFT CEREBRAL ARTERY INFARCTION	S: 11MAY2014 (47) E: 12MAY2014 (48)	AESI	C: 1, 2, 3 D: 12MAY2014	FATAL	UNKNOWN		N/A
Nervous system disorders/ Cerebral ischaemia/ RESPIRATORY INSUFFICIENCY DUE TO LEFTSIDE BRAIN ISCHEMIA	S: 11MAY2014 (47) E: 12MAY2014 (48)	AESI	C: 1, 2, 3 D: 12MAY2014	FATAL	UNKNOWN		N/A

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0107/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS	S: 09DEC2014 (29) E:	AESI	C: 6 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 14DEC2014 (33) E: 25DEC2014 (44)	AESI	C: 6 D: 28NOV2016	RECOVERED/ RESOLVED	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0131/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Subclavian vein thrombosis/ THROMBOSIS OF VENA SUBCLAVIA RIGHT SIDE	S: 16SEP2015 (66) E:	AESI	C: 3 D: 18OCT2017	NOT RECOVERED/NOT RESOLVED	UNKNOWN		RELATED
Vascular disorders/ Thrombophlebitis superficial/ THROMBOSIS OF VENA FEMORALIS SUPERFACIALIS LEFT SIDE	S: 05JUL2017 (724) E: 10JUL2017 (729)	AESI	C: 3 D: 18OCT2017	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Pelvic venous thrombosis/ THROMBOSIS OF VENA ILIACA RIGHT SIDE	S: 23AUG2017 (773) E: 28AUG2017 (778)	AESI	C: 3 D: 18OCT2017	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0138/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Thrombosis/ THROMBOSIS OF V.FEMORALIS COMMUNIS	S: 09FEB2016 (191) E:	AESI	C: 6 D: 06APR2016	NOT RECOVERED/NOT RESOLVED	UNKNOWN		RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 08MAR2016 (219) E:	AESI	C: 3 D: 06APR2016	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0141/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 05AUG2017 (732) E: 09AUG2017 (736)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0175/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 14NOV2016 (70) E:	AESI	C: 3 D:	UNKNOWN	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0176/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 02MAR2017 (168) E: 08MAR2017 (174)	AESI	C: 3 D: 17JAN2019	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 02MAR2017 (168) E: 08MAR2017 (174)	AESI	C: 3 D: 17JAN2019	RECOVERED/ RESOLVED	UNKNOWN		NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0182/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL DISEASE	S: 18JUL2019 (961) E: 24JUL2019 (967)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0185/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Coronary artery thrombosis/ THROMBUS OF LEFT CORONARY ARTERY	S: 15MAR2017 (101) E: 18MAR2017 (104)	AESI	C: 3 D: 20MAY2017	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-093-0209/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 24FEB2019 (700) E: 30MAR2019 (734)	AESI	C: 3 D: 18APR2019	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0018/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 18JAN2017 (548) E: 30JAN2017 (560)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Nervous system disorders/ Cerebrovascular accident/ SUSPECTED APOPLEXY	S: 21SEP2017 (794) E: 29SEP2017 (802)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0019/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ BLEEDING INTRACEREBRAL	S: 07FEB2017 (568) E:	AESI	C: 3 D:	UNKNOWN		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0020/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 05DEC2017 (862) E: 07DEC2017 (864)	AESI	C: 3 D: 27APR2018	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 20MAR2018 (967) E: 31MAR2018 (978)	AESI	C: 3 D: 27APR2018	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0023/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 04APR2016 (197) E: 19APR2016 (212)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0027/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CARDIAC INFARCTION	S: 03MAR2016 (172) E: 04MAR2016 (173)	AESI	C: 6 D: 06NOV2016	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0032/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ SUSPECTED OF HEART ATTACK	S: 22SEP2017 (740) E:	AESI	C: 1 D: 22SEP2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-094-0039/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP LEG VEIN THROMBOSIS LEFT	S: 24JUL2018 (523) E: 20AUG2018 (550)	AESI	C: 3 D: 02NOV2018	RECOVERED/ RESOLVED	DOSE REDUCED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-097-0013/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 01MAR2013 (663) E: 19APR2013 (712)	AESI	C: 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-097-0020/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 28MAR2012 (135) E:	AESI	C: 3 D: 01JAN2014	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-097-0024/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebellar infarction/ PICA CEREBELLUM LACUNA LEFT	S: 24APR2017 (739) E:	AESI	C: 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ BRAIN STROKE, ISCHEMIC BY CAROTIS-STENOSIS	S: 15MAY2017 (760) E:	AESI	C: 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: 23MAY2017 (768) E:	AESI	C: 3, 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		NOT RELATED
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: 23MAY2017 (768) E:	AESI	C: 3, 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NO DATA
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL BLEEDING	S: 23MAY2017 (768) E:	AESI	C: 3, 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		RELATED
Cardiac disorders/ Intracardiac thrombus/ HEART EAR THROMBUS	S: 08DEC2017 (967) E:	AESI	C: 3, 5 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-097-0038/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENT	S: 07OCT2016 (348) E: 11OCT2016 (352)	AESI	C: 6 D: 27MAY2017	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ SUSPECTED ACUTE MYOCARDIAL INFARCTION	S: 13FEB2015 (439) E: 13FEB2015 (439)	AESI	C: 1, 2, 3 D: 13FEB2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0001/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEX INSULT	S: FEB2012 E: FEB2012	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0015/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial thrombosis/ ARTERIAL THROMBOSIS	S: 14MAR2011 (22) E: 22MAR2011 (30)	AESI	C: 1 D: 22MAR2011	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0031/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TIA	S: 05MAY2012 (244) E: 10MAY2012 (249)	AESI	C: 3 D:	RECOVERED/ RESOLVED		NO DATA	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0035/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 12JAN2012 (77) E: 17JAN2012 (82)	AESI	C: 3 D:	RECOVERED/ RESOLVED		NO DATA	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0045/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Iliac artery occlusion/ ILIAC ARTERY OCCLUSION RIGHT LEG	S: 27JUL2012 (219) E: 11AUG2012 (234)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0092/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSITONIC ISCHAEMIC EVENT (TIA)	S: 12NOV2014 (353) E: 12NOV2014 (353)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 25MAY2015 (456) E: 03JUN2015 (465)	AESI	C: 2 D: 21OCT2015	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0112/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Embolic stroke/ MEDIA INFARCTION CARDIOEMBOLIC	S: 13JAN2017 (982) E: 17JAN2017 (986)	AESI	C: 3 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0124/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 07APR2015 (260) E: 10APR2015 (263)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-115-0219/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05SEP2017 (401) E: 17SEP2017 (413)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 11OCT2012 (543) E: 12OCT2012 (544)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-142-0026/68/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ LEFT LEG DEEP THROMBOSIS	S: 03JUN2014 (435) E: 08JUL2014 (470)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 03JUN2014 (435) E: 08JUL2014 (470)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 20NOV2013 (871) E:	AESI	C: 3 D: 29DEC2013	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 29DEC2013 (910) E: 29DEC2013 (910)	AESI	C: 1, 2 D: 29DEC2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-151-0001/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEX DUE TO THROMBOSE	S: 27FEB2013 (294) E: 18MAR2013 (313)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		RELATED
Vascular disorders/ Thrombosis/ APOPLEX DUE TO THROMBOSE	S: 27FEB2013 (294) E: 18MAR2013 (313)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-152-0025/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: E: 09OCT2015 (621)	AESI	C: 1 D: 09OCT2015	FATAL		PERMANENTLY WITHDRAWN	RELATED
Nervous system disorders/ Cerebral infarction/ A. CEREBRI POSTERIOR INFARCTION	S: 19NOV2014 (297) E:	AESI	C: 2, 3, 5 D: 09OCT2015	RECOVERED/ RESOLVED WITH SEQUELAE		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-158-0002/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERY OCCLUSIVE DISEASE	S: 11MAY2012 (316) E:	AESI	C: 3 D: 20DEC2012	NOT RECOVERED/NOT RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-165-0002/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENT	S: E:	AESI	C: 6 D:	UNKNOWN	DOSE NOT CHANGED		RELATED
Cardiac disorders/ Acute myocardial infarction/ NON ELEVATED MYOCARDIAL INFARCTION	S: 03APR2014 (529) E:	AESI	C: 3 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-165-0006/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral ischaemia/ SUSPICIOUS CEREBROVASCULAR ISCHEMIA	S: 14APR2014 (498) E:	AESI	C: 3 D: 23MAY2015	RECOVERING/ RESOLVING	UNKNOWN		NOT RELATED
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY (ACM)	S: 12MAR2015 (830) E:	AESI	C: 3, 5 D: 23MAY2015	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-165-0007/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: E:	AESI	C: 2, 3 D: 21APR2014	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-165-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED
Nervous system disorders/ Cerebral infarction/ SUBACUTE CEREBRAL INFARCTION	S: 30SEP2016 (618) E: 21OCT2016 (639)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-432-0001/74/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI(NON-ST ELEVATION MYOCARDIAL INFARCTION)	S: 09DEC2014 (660) E: 21JAN2015 (703)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE INCREASED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-432-0004/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D:	UNKNOWN	NOT APPLICABLE		NO DATA
Cardiac disorders/ Acute myocardial infarction/ NSEMI	S: 17NOV2013 (364) E: 27NOV2013 (374)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Nervous system disorders/ Cerebral ischaemia/ CEREBRAL ISCHEMIA	S: 10JUN2015 (934) E: 18JUN2015 (942)	AESI	C: 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ FORMALLY NSTEMI	S: 30DEC2012 (14) E: 04JAN2013 (19)	AESI	C: 2, 3 D: 28DEC2014	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Eye disorders/ Retinal infarction/ MACULA INFARCTION LEFT EYE	S: 23NOV2013 (362) E:	AESI	C: 5 D: 11JUL2014	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 03DEC2013 (372) E: 18DEC2013 (387)	AESI	C: 3, 5, 7 D: 11JUL2014	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-432-0020/80/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral embolism/ THROMBEMBOLY LEGS	S: 03SEP2017 (354) E: 05SEP2017 (356)	AESI	C: 2, 3 D: 09DEC2017	RECOVERED/ RESOLVED	DOSE NOT CHANGED		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01MAY2014 (318) E: 11MAY2014 (328)	AESI	C: 1 D: 11MAY2014	FATAL		NO DATA	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-454-0042/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 25JUN2016 (373) E: 26JUN2016 (374)	AESI	C: 2 D: 07OCT2016	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-463-0008/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Basal ganglia haemorrhage/ BASAL GANGLIA HEMORRHAGE RIGHT	S: E: 01JUL2014 (488)	AESI	C: 1, 2 D: 01JUL2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED
Injury, poisoning and procedural complications/ Subdural haematoma/ SUBDURAL HEMATOMA RIGHT	S: E: 01JUL2014 (488)	AESI	C: 1, 2 D: 01JUL2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-463-0015/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06DEC2013 (102) E:	AESI	C: 1 D: 06DEC2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-471-0015/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY ARTERY EMBOLISM	S: 01SEP2014 (97) E: 09DEC2014 (196)	AESI	C: 1 D: 09DEC2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-471-0016/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: E:	AESI	C: 1, 2 D: 19SEP2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-471-0033/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ DECOMPENSATION CHRONIC RIGHT HEART FAILURE AND HEART ATTACK	S: 08DEC2016 (731) E:	AESI	C: 1 D: 08DEC2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Ge-471-0041/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 30JUN2016 (444) E:	AESI	C: 3, 6 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 29OCT2014 (164) E: 31OCT2014 (166)	AESI	C: 1, 2 D: 31OCT2014	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22FEB2015 (256) E: 26FEB2015 (260)	AESI	C: 1, 2, 3 D: 26FEB2015	FATAL		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 18MAR2014 (297) E: 18MAR2014 (297)	AESI	C: 1, 2 D: 18MAR2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 15MAY2014 (92) E: 15MAY2014 (92)	AESI	C: 2 D: 13SEP2014	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D: 05JUL2015	UNKNOWN	UNKNOWN		NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ ACUTE CORONARY INFARCTION	S: 05JUL2015 (754) E: 05JUL2015 (754)	AESI	C: 1 D: 05JUL2015	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 28SEP2014 (423) E:	AESI	C: 2, 3 D:	UNKNOWN	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21AUG2013 (149) E: 21AUG2013 (149)	AESI	C: 1, 2, 3 D: 21AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 05APR2016 (407) E:	AESI	C: 1, 2 D: 05APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ VASCULAR STROKE	S: 14OCT2015 (233) E:	AESI	C: 1, 2 D: 14OCT2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: E: 14JAN2015 (178)	AESI	C: 1, 3 D: 14JAN2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: AUG2017 E:	AESI	C: 1 D: 20AUG2017	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 30AUG2013 (99) E: 30AUG2013 (99)	AESI	C: 1, 2, 3 D: 30AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: 03JUN2014 (288) E:	AESI	C: 1, 6 D: 03JUL2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20OCT2013 (7) E:	AESI	C: 1 D: 29OCT2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 14OCT2014 (272) E: 23OCT2014 (281)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: 14OCT2014 (272) E: 23OCT2014 (281)	AESI	C: 2, 3, 6 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART ATTACK	S: 07JUL2016 (144) E:	AESI	C: 1 D: 07JUL2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24NOV2016 (231) E:	AESI	C: 1, 2, 3 D: 24NOV2016	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 24JUL2015 (523) E: 31JUL2015 (530)	AESI	C: 1, 2, 3 D: 31JUL2015	FATAL	DOSE REDUCED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 30DEC2015 (658) E: 01JAN2016 (660)	AESI	C: 1 D: 01JAN2016	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Gr-059-0006/46/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ HEART INFARCTION	S: 10FEB2017 (122) E:	AESI	C: 1 D: 10FEB2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 05NOV2015 (43) E: 05NOV2015 (43)	AESI	C: 1 D: 05NOV2015	FATAL	NOT APPLICABLE		N/A

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Gr-065-0005/86/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CORONARY INFARCTION	S: E:	AESI	C: 1 D: 29OCT2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMIACS	S: 12MAY2014 (453) E:	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-022-0018/61/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	C: 6 D:	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-038-0002/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 17SEP2012 (405) E:	AESI	C: 3, 5 D: 04JAN2014	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-038-0014/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Haemorrhagic stroke/ HAEMORRHAGIC ICTUS	S: 09AUG2012 (7) E: 11AUG2012 (9)	AESI	C: 1, 2, 3 D: 11AUG2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 27NOV2017 (887) E:	AESI	C: 3 D: 22DEC2017	NOT RECOVERED/NOT RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-073-0027/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS	S: 06APR2018 (620) E: MAY2018	AESI	C: 3, 6 D:	RECOVERED/ RESOLVED		POST-THERAPY	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-084-0001/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 13DEC2011 (198) E: 21DEC2011 (206)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-087-0004/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 06SEP2012 (315) E: 25FEB2013 (487)	AESI	C: 6 D:	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: E: 07APR2014 (67)	AESI	C: 1 D: 07APR2014	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-093-0005/77/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 02SEP2013 (186) E:	AESI	C: 1 D: 02SEP2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-093-0008/70/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Dermatitis atopic/ ATOPIC DERMATITIS	S: 22AUG2013 (36) E:	ADR	C: 6 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 19MAR2016 (858) E:	AESI	C: 1 D: 19MAR2016	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-116-0021/70/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: E: 13NOV2014 (352)	AESI	C: 1 D: 13NOV2014	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-116-0022/76/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 09FEB2015 (437) E:	AESI	C: 3, 5 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

It-116-0024/85/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular disorder/ CEREBROVASCULAR EVENT	S: 20MAR2014 (15) E:	AESI	C: 1 D: 20MAR2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Blood and lymphatic system disorders/ Aplasia pure red cell/ PURE RED CELL APLASIA	S: 21FEB2015 (250) E: 28APR2016 (682)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 21FEB2015 (250) E: 28APR2016 (682)	AESI	C: 2, 3 D:	NOT RECOVERED/NOT RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ CEREBRAL STROKE	S: 04NOV2014 (114) E: 15DEC2014 (155)	AESI	C: 1, 2, 3 D: 15DEC2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 26AUG2017 (970) E: 26AUG2017 (970)	AESI	C: 1 D: 30AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 30OCT2014 (991) E:	AESI	C: 2, 3 D: 28DEC2014	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21MAR2012 (38) E: 30MAR2012 (47)	AESI	C: 2 D: 11JAN2014	RECOVERED/ RESOLVED		NO DATA	NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 09JAN2014 (697) E: 11JAN2014 (699)	AESI	C: 1, 2, 3 D: 11JAN2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22NOV2013 (648) E: 24NOV2013 (650)	AESI	C: 1, 2 D: 24NOV2013	FATAL	NOT APPLICABLE		NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MINOR MYOCARDIAL INFARCTION	S: 04SEP2015 (722) E:	AESI	C: 2 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 04APR2016 (935) E: 13MAY2016 (974)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CARDIAC INFARCTION (TYPE 2)	S: 24AUG2015 (651) E: 28AUG2015 (655)	AESI	C: 2, 3 D: 26SEP2015	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ MYOCARDIAL INFARCTION (NSTEMI)	S: 20FEB2015 (290) E:	AESI	C: 2, 3 D: 05APR2015	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HEMORRHAGE	S: 08MAY2015 (367) E:	AESI	C: 2, 3 D: 03DEC2015	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE INFARCTION	S: 26APR2016 (610) E:	AESI	C: 1 D: 26APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 14NOV2015 (443) E: 30DEC2015 (489)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT CEREBRAL ISCHEMIC ATTACK	S: 27JAN2016 (517) E: 28JAN2016 (518)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PROB. PULMONARY EMBOLISM	S: 22DEC2016 (847) E:	AESI	C: 2, 3 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Embolic cerebral infarction/ EMBOLIC CEREBRAL INFARCTION	S: 24JUL2015 (325) E:	AESI	C: 2, 3 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NO DATA

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MI	S: 27JUL2017 (557) E:	AESI	C: 2, 6 D: 27DEC2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 10OCT2013 (115) E: 14OCT2013 (119)	AESI	C: 2, 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ CARDIAC INFACTION	S: 03JUN2016 (932) E: 07JUN2016 (936)	AESI	C: 1, 2, 3 D: 07JUN2016	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 02NOV2017 (954) E:	AESI	C: 2, 3 D: 07JAN2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	NO DATA
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	NOT RELATED
Nervous system disorders/ Cerebral haemorrhage/ INTRACEREBRAL HEMORRHAGE	S: 06JAN2018 (1019) E:	AESI	C: 1, 2, 3, 5 D: 07JAN2018	FATAL		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NSTEMI	S: 04MAY2019 (1031) E: 07MAY2019 (1034)	AESI	C: 3 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20DEC2012 (16) E: 20DEC2012 (16)	AESI	C: 1, 3 D: 20DEC2012	FATAL	NOT APPLICABLE		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 06MAR2015 (670) E: 06MAR2015 (670)	AESI	C: 6 D: 07JUN2015	RECOVERED/ RESOLVED	UNKNOWN		RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01JUN2015 (757) E: 07JUN2015 (763)	AESI	C: 1, 2 D: 07JUN2015	FATAL	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01OCT2014 (475) E: 10OCT2014 (484)	AESI	C: 3 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 03APR2011 (77) E: 15APR2011 (89)	AESI	C: 3, 7 D: 03SEP2012	RECOVERED/ RESOLVED	UNKNOWN		NOT ASSESSABLE
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 03SEP2012 (596) E:	AESI	C: 1, 3, 7 D: 03SEP2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ NON ST SEGMENT ELEVATION MYOCARDIAL INFARCTION	S: 09MAY2011 (111) E:	AESI	C: 2, 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 09DEC2011 (324) E:	AESI	C: 1, 2, 3, 7 D: 09DEC2011	FATAL	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 19JUL2011 (183) E: 25JUL2011 (189)	AESI	C: 2, 3, 7 D: 23DEC2013	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ MEDULLA OBLONGATA BLEEDING	S: 13MAR2011 (55) E:	AESI	C: 1, 3, 7 D: 13MAR2011	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 07FEB2012 (385) E: 18FEB2012 (396)	AESI	C: 2, 3, 7 D: 20FEB2013	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 13MAR2011 (54) E: 21MAR2011 (62)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Haemorrhagic stroke/ HEMORRHAGIC STROKE	S: 19DEC2011 (335) E: 29DEC2011 (345)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS OF THE LOWER LEFT LIMB	S: 27APR2014 (1165) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 14OCT2012 (608) E:	AESI	C: 1, 3, 7 D: 14OCT2012	FATAL	UNKNOWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01JUL2014 (411) E:	AESI	C: 1, 2, 3, 7 D: 01JUL2014	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 29APR2011 (89) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Arteriovenous fistula occlusion/ FISTULA OCCLUSION	S: 27SEP2013 (1005) E: 28SEP2013 (1006)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Injury, poisoning and procedural complications/ Arteriovenous fistula occlusion/ FISTULA OCCLUSION	S: 30SEP2013 (1008) E: 01OCT2013 (1009)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Injury, poisoning and procedural complications/ Arteriovenous fistula occlusion/ FISTULA OCCLUSION	S: 15OCT2013 (1023) E: 16OCT2013 (1024)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
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System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism arterial/ THROMBOEMBOLIC OCCLUSION OF FEMORAL ARTERY WITH CRITICAL ISCHAEMIA OF LEFT LEG.	S: 21SEP2018 (185) E:	AESI	C: 1, 2, 3, 7 D: 21SEP2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 30AUG2013 (326) E: 02SEP2013 (329)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 16DEC2013 (434) E: 18DEC2013 (436)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 23APR2014 (562) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE INCREASED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
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Epoetin Zeta C1111006 (EPOE-09-11) and PMS-830-09-0082
Listing of Serious Adverse Events (Protocol Defined AESI or ADR)
Safety Analysis Set

De-006-B003/C/M
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		NOT RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 22JAN2013 (200) E: 24JAN2013 (202)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: AUG2013 E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 11FEB2014 (730) E: 15FEB2014 (734)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 26APR2014 (804) E: 28APR2014 (806)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
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PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS OF THE LOWER LIMBS	S: 01FEB2013 (207) E: 15FEB2013 (221)	AESI	C: 3, 7 D: 13OCT2013	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 13OCT2013 (461) E:	AESI	C: 1, 3, 7 D: 13OCT2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Eye disorders/ Retinal artery occlusion/ CENTRAL RETINAL ARTERY OCCLUSION OF LEFT EYE	S: 23NOV2012 (250) E: 29NOV2012 (256)	AESI	C: 3, 5, 7 D: 27JUL2014	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 30JAN2013 (318) E: 15FEB2013 (334)	AESI	C: 3, 7 D: 27JUL2014	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 26JUN2016 (537) E:	AESI	C: 3, 5, 7 D: 15SEP2016	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 11NOV2014 (818) E:	AESI	C: 1, 2, 3, 7 D: 11NOV2014	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 15OCT2017 (964) E:	AESI	C: 1, 2, 3, 7 D: 15OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 14NOV2012 (134) E:	AESI	C: 1, 7 D: 14NOV2012	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 08DEC2015 (524) E: 08DEC2015 (524)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT DYSFUNCTION OF UPPER ARM SHUNT LEFT	S: 09JUL2014 (216) E: 12JUL2014 (219)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 29JUL2014 (280) E: 01AUG2014 (283)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 21AUG2015 (668) E: 21AUG2015 (668)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 05SEP2015 (684) E: 15SEP2015 (694)	AESI	C: 3, 7 D: 02NOV2015	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Investigations/ Haemoglobin decreased/ HAEMOGLOBIN VALUES DECREASED TO 8.4 G/DL	S: APR2015 E:	ADR	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 28APR2015 (554) E:	AESI	C: 6, 7 D:	UNKNOWN	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 25NOV2014 (399) E: 29NOV2014 (403)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 28DEC2014 (432) E: 20JAN2015 (455)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		UNLIKELY RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 23OCT2015 (731) E: 03NOV2015 (742)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		UNLIKELY RELATED
Nervous system disorders/ Cerebrovascular accident/ ARTERIA CEREBRI MEDIA LEFT SYMPTOM	S: 02AUG2016 (1015) E: 04AUG2016 (1017)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 30JUN2011 (2) E: 04JUL2011 (6)	AESI	C: 2, 3, 7 D: 13NOV2012	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ RIGHT SIDED PULMONARY EMBOLISM	S: 12JAN2012 (240) E: 27JAN2012 (255)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 20NOV2012 (670) E: 21NOV2012 (671)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 16DEC2013 (1063) E:	AESI	C: 1, 2, 3, 7 D: 17DEC2013	FATAL	NOT APPLICABLE		UNLIKELY RELATED
Gastrointestinal disorders/ Mesenteric vein thrombosis/ MESENTERIC THROMBOSIS	S: 17DEC2013 (1064) E:	AESI	C: 1, 2, 3, 7 D: 17DEC2013	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ THROMBOSED SHUNT ANEURYSM OF THE LEFT ARM	S: 03MAY2011 (102) E: 04MAY2011 (103)	AESI	C: 3, 7 D: 23AUG2011	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 23AUG2011 (214) E:	AESI	C: 1, 3, 7 D: 23AUG2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	C: 1, 7 D: 01APR2011	FATAL	DRUG WITHDRAWN		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	C: 1, 7 D: 01APR2011	FATAL	UNKNOWN		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 01APR2011 (73) E:	AESI	C: 1, 7 D: 01APR2011	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 16SEP2011 (115) E:	AESI	C: 1, 7 D: 16SEP2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 27JUN2013 (879) E: 10JUL2013 (892)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Vascular disorders/ Arterial occlusive disease/ ACUTE ARTERIAL OCCLUSION LEFT LOWER LEG	S: 10SEP2013 (954) E: 16SEP2013 (960)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Eye disorders/ Retinal vein thrombosis/ CENTRAL VEIN THROMBOSIS OF LEFT EYE	S: MAR2011 E: MAR2011	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 07AUG2011 (39) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 19DEC2012 (624) E:	AESI	C: 2, 3, 7 D:	UNKNOWN	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS OF THE LOWER LIMBS	S: 01APR2011 (19) E: 30APR2011 (48)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 15JUL2012 (418) E: 26JUL2012 (429)	AESI	C: 3, 7 D: 25FEB2013	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26DEC2011 (120) E:	AESI	C: 1, 7 D: 26DEC2011	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS IN HIS LEFT LEG	S: 12JUL2012 (84) E: 19JUL2012 (91)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACKS	S: 15DEC2013 (791) E: 15JAN2014 (822)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Eye disorders/ Retinal vein thrombosis/ VENOUS THROMBOSIS OF RIGHT EYE	S: 01FEB2012 (80) E: 20APR2012 (159)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01SEP2011 (197) E:	AESI	C: 1, 7 D: 01SEP2011	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05MAY2012 (443) E:	AESI	C: 1, 7 D: 05MAY2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Arrhythmia/ ARRHYTHMIA	S: 21MAR2012 (58) E:	ADR	C: 2, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED
Nervous system disorders/ Dizziness/ DIZZINESS	S: 21MAR2012 (58) E:	ADR	C: 2, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED
Nervous system disorders/ Somnolence/ DROWSINESS	S: 21MAR2012 (58) E:	ADR	C: 2, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22MAY2017 (608) E: 01JUN2017 (618)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 10APR2017 (1142) E: 14APR2017 (1146)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: E:	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 04JAN2012 (224) E: 04JAN2012 (224)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 06JUL2012 (408) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 17JUN2014 (1052) E:	AESI	C: 1, 2, 3, 7 D: 17JUN2014	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebellar haematoma/ SUBDURAL HEMATOMA AT CEREBELLUM (BRAIN HEMORRHAGE)	S: 15MAY2014 (886) E: 28MAY2014 (899)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DRUG WITHDRAWN		UNLIKELY RELATED
Nervous system disorders/ Cerebellar haematoma/ SUBDURAL HEMATOMA AT CEREBELLUM (BRAIN HEMORRHAGE)	S: 15MAY2014 (886) E: 28MAY2014 (899)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		POSSIBLE RELATED
Nervous system disorders/ Cerebellar haematoma/ SUBDURAL HEMATOMA AT CEREBELLUM (BRAIN HEMORRHAGE)	S: 15MAY2014 (886) E: 28MAY2014 (899)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		POSSIBLE RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 23JUL2014 (955) E:	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DRUG WITHDRAWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 09OCT2011 (157) E: 09OCT2011 (157)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERY OCCLUSIVE DISEASE WITH LOWER LEG GANGRENE	S: 28MAY2013 (677) E:	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 22AUG2012 (391) E: 15SEP2012 (415)	AESI	C: 3, 7 D: 01FEB2013	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 19MAY2013 (662) E: 31MAY2013 (674)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05JUL2012 (448) E:	AESI	C: 1, 3, 7 D: 05JUL2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05MAR2012 (313) E: 14MAR2012 (322)	AESI	C: 2, 3, 7 D: 13FEB2014	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 23MAR2012 (331) E: 04APR2012 (343)	AESI	C: 2, 3, 7 D: 13FEB2014	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 25AUG2013 (861) E: 04OCT2013 (901)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNKNOWN

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 28JUL2015 (179) E:	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ UNSPECIFIED STROKE	S: 27OCT2011 (196) E: 16NOV2011 (216)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 05SEP2011 (146) E:	AESI	C: 3, 7 D: 30NOV2011	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE OF THE LEGS	S: 09JAN2015 (464) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE OF THE LEGS	S: 05MAR2015 (519) E:	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 18FEB2014 (369) E: 18FEB2014 (369)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 12DEC2014 (288) E: 16DEC2014 (292)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ APOPLEXY	S: 01JUL2019 (442) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24MAY2019 (288) E:	AESI	C: 1, 2, 3, 7 D: 24MAY2019	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 06JAN2016 (758) E: 08JAN2016 (760)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 21JUL2015 (60) E: 23JUL2015 (62)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT ASSESSABLE
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACKS	S: 21SEP2016 (488) E: 24SEP2016 (491)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE OF HIS LEGS	S: 07JAN2014 (1001) E: 25JAN2014 (1019)	AESI	C: 1, 3, 7 D: 25JAN2014	FATAL	DRUG WITHDRAWN		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 10NOV2013 (80) E: 22NOV2013 (92)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 02NOV2012 (404) E: 08NOV2012 (410)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 23DEC2013 (820) E: 27DEC2013 (824)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 17MAY2014 (965) E: 21MAY2014 (969)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 04SEP2014 (434) E: 05SEP2014 (435)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ ASSUMED ARTERIAL OCCLUSION DISEASE	S: 15NOV2019 (862) E: 23NOV2019 (870)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS OF THE LOWER LIMBS	S: 12JUL2014 (118) E: 23JUL2014 (129)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE	S: 27JAN2014 (952) E:	AESI	C: 3, 5, 7 D:	NOT RECOVERED/NOT RESOLVED	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 16APR2012 (18) E:	AESI	C: 1, 3, 5, 7 D: 13JAN2014	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 25AUG2016 (563) E:	AESI	C: 3, 7 D: 04OCT2016	NOT RECOVERED/NOT RESOLVED	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL DISEASE STAGE IV	S: 08AUG2013 (790) E: 24SEP2013 (837)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE INCREASED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Subdural haematoma/ SUBDURAL HAEMATOMA	S: 30OCT2013 (811) E: 11NOV2013 (823)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 08DEC2011 (235) E:	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DRUG WITHDRAWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSION AT KNOWN PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 22NOV2016 (610) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04APR2016 (132) E: 06APR2016 (134)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ DETERIORATION OF A PREEXISTING PERIPHERAL ARTERIAL DISEASE	S: 25JAN2014 (71) E:	AESI	C: 3, 5, 7 D:	UNKNOWN	UNKNOWN		NOT RELATED
Vascular disorders/ Arterial occlusive disease/ OCCLUSION OF ARTERIA FEMORALIS COMMUNIS	S: 12NOV2014 (362) E: 12DEC2014 (392)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 16NOV2012 (446) E: 16NOV2012 (446)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
	S: 14MAY2014 (547) E: 17JUN2014 (581)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 27NOV2014 (30) E: 04JAN2015 (68)	AESI	C: 2, 3, 7 D: 22MAY2016	UNKNOWN	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 06FEB2013 (29) E:	AESI	C: 3, 7 D:	UNKNOWN	UNKNOWN		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 15APR2013 (97) E: 15APR2013 (97)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20OCT2011 (95) E:	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		NOT RELATED
Vascular disorders/ Arterial occlusive disease/ OCCLUSION OF 2 LOWER LEG ARTERIES	S: 23MAR2012 (250) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 23MAR2012 (250) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 02FEB2012 (169) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE INCREASED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04JUL2016 (301) E:	AESI	C: 1, 2, 3, 7 D: 04JUL2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 31MAR2014 (890) E:	AESI	C: 3, 7 D: 15JAN2015	UNKNOWN	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 16DEC2013 (685) E: 17JAN2014 (717)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 29JUL2013 (720) E:	AESI	C: 3, 7 D:	UNKNOWN	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18JUL2012 (154) E:	AESI	C: 1, 7 D: 18JUL2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 18FEB2012 (15) E: 14MAR2012 (40)	AESI	C: 3, 7 D: 03NOV2014	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 05JUL2014 (883) E: 30JUL2014 (908)	AESI	C: 3, 7 D: 03NOV2014	RECOVERED/ RESOLVED	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE STAGE III	S: 16AUG2012 (182) E: 28AUG2012 (194)	AESI	C: 3, 5, 7 D: 05MAY2014	RECOVERED/ RESOLVED WITH SEQUELAE	UNKNOWN		UNLIKELY RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 09OCT2012 (236) E: 09OCT2012 (236)	AESI	C: 3, 7 D: 05MAY2014	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 30JUL2012 (178) E: 11AUG2012 (190)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ DETERIORATION OF PREEXISTING PERIPHERAL ARTERIAL OCCLUSIVE DISEASE GRADE IV	S: 02SEP2014 (942) E:	AESI	C: 3, 5, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 17MAR2013 (397) E: 18APR2013 (429)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Mesenteric artery stenosis/ HIGH GRADE STENOSIS OF ARTERIA MESENTERICA SUPERIOR	S: 25JUN2012 (130) E: 05JUL2012 (140)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 05SEP2012 (204) E: 08SEP2012 (207)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE REDUCED		UNLIKELY RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ THROMBOSIS OF VENA BRACHIOCEPHALICA	S: 10OCT2012 (239) E: 13OCT2012 (242)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE REDUCED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Angioedema/ QUINCKE'S EDEMA	S: 10NOV2015 (83) E: 15NOV2015 (88)	ADR	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED
Skin and subcutaneous tissue disorders/ Angioedema/ QUINCKE'S EDEMA	S: 10NOV2015 (83) E: 15NOV2015 (88)	ADR	C: 6, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ BILATERAL PULMONARY EMBOLISM	S: 29AUG2015 (9) E:	AESI	C: 2, 3, 7 D:	NOT RECOVERED/NOT RESOLVED	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 28NOV2011 (117) E: 24DEC2011 (143)	AESI	C: 3, 7 D: 01FEB2014	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 02MAR2012 (212) E: 08MAR2012 (218)	AESI	C: 2, 3, 7 D: 01FEB2014	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01FEB2014 (913) E:	AESI	C: 1, 2, 3, 7 D: 01FEB2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 21SEP2012 (388) E: 28SEP2012 (395)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Aortic thrombosis/ THROMBOSIS OF AORTA DESCENDES	S: 02JUL2013 (126) E:	AESI	C: 5, 7 D: 09MAR2014	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ INCREASED PROGRESSIVE PERIPHERAL ARTERIAL DISEASE	S: 02JAN2014 (310) E:	AESI	C: 3, 7 D: 09MAR2014	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Investigations/ Haemoglobin decreased/ HEMOGLOBIN LEVEL WAS DECREASED	S: E:	ADR	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED
Investigations/ Haemoglobin decreased/ HEMOGLOBIN LEVEL WAS DECREASED	S: E:	ADR	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		POSSIBLE RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 28MAY2014 (720) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 28MAY2014 (720) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHAEMIC ATTACK	S: 13AUG2016 (654) E: 20AUG2016 (661)	AESI	C: 3, 7 D: 06JAN2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 01JUL2012 (308) E:	AESI	C: 1, 7 D: 01JUL2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 15NOV2016 (83) E:	AESI	C: 5, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE GRADE IIB	S: 01APR2015 (1227) E: 04APR2015 (1230)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED
Vascular disorders/ Arterial occlusive disease/ ARTERIAL OCCLUSIVE DISEASE	S: 07MAY2015 (1263) E:	AESI	C: 3, 5, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED
Cardiac disorders/ Coronary artery occlusion/ OCCLUSION OF ARTERIA CORONARIA DEXTRA	S: 07MAY2015 (1263) E:	AESI	C: 3, 5, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ DIALYSIS SHUNT OCCLUSION	S: 27NOV2014 (1025) E: 27NOV2014 (1025)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 17NOV2017 (172) E: 19NOV2017 (174)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ ACUTE SHUNT OCCLUSION OF LEFT ARM	S: 27MAY2017 (1009) E: 27MAY2017 (1009)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 31JAN2013 (521) E: 07FEB2013 (528)	AESI	C: 2, 3, 7 D: 18MAR2013	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18MAR2013 (567) E:	AESI	C: 1, 2, 3, 7 D: 18MAR2013	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ MISSING HAEMOGLOBIN INCREASE	S: 14NOV2016 (82) E: 06DEC2016 (104)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24MAR2014 (740) E: 03APR2014 (750)	AESI	C: 3, 7 D: 11DEC2014	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04DEC2012 (156) E: 10DEC2012 (162)	AESI	C: 1, 3, 7 D: 10DEC2012	FATAL	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 13AUG2013 (587) E:	AESI	C: 1, 3, 7 D: 13AUG2013	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Venous occlusion/ VENOUS OCCLUSION OF ARTERIA BRACHIALIS LEFT	S: 03JAN2014 (563) E:	AESI	C: 1, 3, 7 D: 03JAN2014	FATAL	DOSE NOT CHANGED		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 07MAY2012 (165) E: 23MAY2012 (181)	AESI	C: 1, 2, 3, 7 D: 23SEP2014	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 23SEP2014 (1034) E:	AESI	C: 1, 2, 3, 7 D: 23SEP2014	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial occlusive disease/ OCCLUSION OF ARTERY TIBIALIS POSTERIOR LEFT	S: 13MAY2013 (497) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ PULMONARY EMBOLISM	S: 18APR2013 (164) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MILD MYOCARDIAL INFARCTION (NSTEMI)	S: 02MAY2014 (543) E: 02MAY2014 (543)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HAEMORRHAGE	S: 16DEC2012 (273) E:	AESI	C: 1, 2, 3, 7 D: 16DEC2012	FATAL	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ DYSFUNCTION OF THE LONG-TERM CENTRAL VENOUS CATHETER	S: 02JAN2013 (161) E: 03JAN2013 (162)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 04JUL2015 (788) E:	AESI	C: 1, 7 D: 04JUL2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 30JUL2013 (379) E: 04AUG2013 (384)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 17OCT2016 (358) E:	AESI	C: 1, 2, 3, 7 D: 17OCT2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Infections and infestations/ Gangrene/ GANGRENE OF TOES	S: 13DEC2017 (43) E:	ADR	C: 1, 2, 3, 7 D: 13DEC2017	FATAL	NOT APPLICABLE		POSSIBLE RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PROGRESSION OF PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 13DEC2017 (43) E:	AESI	C: 1, 2, 3, 7 D: 13DEC2017	FATAL	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 14AUG2017 (659) E: 16AUG2017 (661)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 14AUG2017 (659) E: 16AUG2017 (661)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ DIALYSIS SHUNT OCCLUSION	S: 23SEP2013 (174) E: 23SEP2013 (174)	AESI	C: 6, 7 D: 28OCT2013	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Coronary artery occlusion/ CORONARY OCCLUSION OF RIGHT CORONARY ARTERY	S: 06AUG2019 (648) E: 07AUG2019 (649)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral artery occlusion/ OCCLUSION OF SUPERFICIAL FEMORAL ARTERY LEFT	S: 19JUN2017 (602) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: E:	AESI	C: 6, 7 D:	UNKNOWN	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ STROKE	S: 20JUN2014 (195) E: 21JUN2014 (196)	AESI	C: 3, 5, 7 D:	UNKNOWN	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 07APR2016 (143) E:	AESI	C: 1, 2, 3, 7 D: 07APR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral artery occlusion/ EMBOLIC OCCLUSION OF ARTERIA POPLITEA LEFT	S: 19JUN2017 (727) E: 21JUN2017 (729)	AESI	C: 3, 7 D: 04JAN2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 23OCT2017 (853) E: 17NOV2017 (878)	AESI	C: 2, 3, 5, 7 D: 04JAN2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 19FEB2016 (122) E: 26FEB2016 (129)	AESI	C: 3, 7 D: 20APR2016	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18APR2017 (514) E: 18APR2017 (514)	AESI	C: 2, 3, 7 D: 18AUG2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Peripheral embolism/ ARTERIAL EMBOLISM OF RIGHT FOOT	S: 18AUG2018 (1001) E:	AESI	C: 1, 3, 7 D: 18AUG2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 23JUL2015 (207) E:	AESI	C: 1, 2, 7 D: 23JUL2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11FEB2016 (116) E:	AESI	C: 1, 2, 3, 7 D: 11FEB2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 19JUL2016 (299) E: 25JUL2016 (305)	AESI	C: 3, 7 D: 10AUG2017	RECOVERED/ RESOLVED	DOSE INCREASED		UNLIKELY RELATED
Vascular disorders/ Arterial occlusive disease/ PROGRESSIVE ARTERIAL OCCLUSIVE DISEASE	S: 10AUG2017 (686) E:	AESI	C: 1, 2, 3, 7 D: 10AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 17FEB2016 (575) E: 08APR2016 (626)	AESI	C: 2, 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06DEC2015 (684) E: 16DEC2015 (694)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 02JUN2015 (495) E:	AESI	C: 1, 2, 7 D: 02JUN2015	FATAL	NOT APPLICABLE		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 24AUG2015 (215) E:	AESI	C: 1, 3, 7 D: 24AUG2015	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Respiratory, thoracic and mediastinal disorders/ Pulmonary embolism/ LUNG EMBOLISM	S: 17SEP2014 (134) E: 11OCT2014 (158)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INADEQUATE LOW HAEMOGLOBIN CONCENTRATION (LACK OF DRUG EFFECT)	S: 31OCT2019 (681) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE INCREASED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 03AUG2015 (68) E: 06AUG2015 (71)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26AUG2015 (91) E: 09SEP2015 (105)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 10SEP2015 (106) E: 16SEP2015 (112)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 28DEC2015 (215) E: 30DEC2015 (217)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26FEB2016 (275) E: 09MAR2016 (287)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 16JUN2016 (386) E: 24JUN2016 (394)	AESI	C: 2, 3, 5, 7 D: 09DEC2016	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 09DEC2016 (562) E:	AESI	C: 1, 2, 3, 7 D: 09DEC2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 14JUN2015 (65) E: 27JUN2015 (78)	AESI	C: 3, 7 D: 15MAR2017	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ CEREBRAL INFARCTION OF LEFT MIDDLE CEREBRAL ARTERY	S: 03JAN2017 (620) E: 14JAN2017 (631)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21JUN2015 (69) E:	AESI	C: 1, 2, 7 D: 21JUN2015	FATAL	NOT APPLICABLE		NOT ASSESSABLE

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21SEP2015 (197) E:	AESI	C: 1, 2, 3, 7 D: 21SEP2015	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 07AUG2016 (558) E: 08AUG2016 (559)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 28NOV2016 (671) E:	AESI	C: 6, 7 D:	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED
Investigations/ Haemoglobin decreased/ HAEMOGLOBIN DECREASE	S: 28NOV2016 (671) E:	ADR	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INSUFFICIENT HAEMOGLOBIN INCREASE (LACK OF DRUG EFFECT)	S: 10AUG2015 (155) E: 07SEP2015 (183)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 12DEC2017 (490) E: 29JAN2018 (538)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED
Investigations/ Haemoglobin decreased/ HAEMOGLOBIN DECREASE	S: 12DEC2017 (490) E: 29JAN2018 (538)	ADR	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INSUFFICIENT HAEMOGLOBIN INCREASE (LACK OF DRUG EFFECT)	S: 27NOV2017 (1023) E: 08JAN2018 (1065)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INSUFFICIENT HAEMOGLOBIN INCREASE (LACK OF DRUG EFFECT)	S: 27DEC2017 (115) E: 27DEC2017 (115)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Hypertensive urgency/ HYPERTENSIVE URGENCY	S: 28DEC2015 (179) E:	ADR	C: 6, 7 D:	UNKNOWN	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Surgical and medical procedures/ Arterial stent insertion/ STENT SURGERY OF ARTERIA FEMORALIS SUPERFICIALIS	S: 15FEB2017 (531) E: 22MAR2017 (566)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 16AUG2017 (114) E: 25AUG2017 (123)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE INCREASED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 30MAY2016 (238) E:	AESI	C: 1, 2, 3, 7 D: 30MAY2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS OF THE RIGHT LEG	S: 20JUL2016 (195) E: 30JUL2016 (205)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ NO DRUG EFFECT	S: 16MAY2018 (702) E:	AESI	C: 6, 7 D:	UNKNOWN	DRUG WITHDRAWN		PROBABLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 07MAR2018 (797) E:	AESI	C: 2, 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral ischaemia/ ACUTE CEREBRAL ISCHAEMIA	S: 08MAR2017 (454) E: 12MAR2017 (458)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 27JUN2018 (911) E: 20JUL2018 (934)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Acute myocardial infarction/ ACUTE MYOCARDIAL INFARCTION	S: 20JUL2017 (535) E:	AESI	C: 1, 2, 3, 7 D: 20JUL2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11DEC2017 (708) E: 24DEC2017 (721)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 12MAY2018 (831) E:	AESI	C: 1, 2, 7 D: 12MAY2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHAEMIC ATTACK	S: 01JAN2016 (52) E: 01JAN2016 (52)	AESI	C: 2, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06JAN2017 (423) E: 06JAN2017 (423)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 12MAY2017 (563) E: 12MAY2017 (563)	AESI	C: 1, 3, 7 D: 12MAY2017	FATAL	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 23JUL2016 (93) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 05JUL2017 (442) E: 05JUL2017 (442)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 14JAN2017 (269) E: 14JAN2017 (269)	AESI	C: 2, 3, 7 D: 17OCT2017	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE FONTAINE STAGE IV	S: 17OCT2017 (545) E:	AESI	C: 1, 2, 3, 7 D: 17OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 12JUN2018 (782) E:	AESI	C: 1, 2, 7 D: 12JUN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 14AUG2017 (607) E:	AESI	C: 1, 2, 3, 7 D: 14AUG2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 16OCT2017 (674) E:	AESI	C: 1, 2, 3, 7 D: 16OCT2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 01FEB2016 (25) E:	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 06JAN2018 (723) E:	AESI	C: 1, 2, 3, 7 D: 06JAN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE STAGE IV FEMEROPOPLITEAL WITH GANGRENE.	S: 29MAR2018 (832) E:	AESI	C: 3, 7 D: 26JUN2018	RECOVERED/ RESOLVED WITH SEQUELAE	NOT APPLICABLE		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26JUN2018 (921) E:	AESI	C: 1, 2, 3, 7 D: 26JUN2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 13MAR2016 (96) E:	AESI	C: 1, 2, 3, 7 D: 13MAR2016	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ CEREBRAL HEMORRHAGE	S: 04NOV2016 (332) E:	AESI	C: 1, 2, 3, 7 D: 04NOV2016	FATAL	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 18MAY2017 (488) E: 22MAY2017 (492)	AESI	C: 3, 7 D: 29AUG2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 08SEP2016 (274) E:	AESI	C: 3, 5, 7 D: 29SEP2017	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 29SEP2017 (660) E:	AESI	C: 1, 2, 3, 7 D: 29SEP2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE STAGE IV	S: 11OCT2018 (988) E:	AESI	C: 3, 7 D: 21DEC2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Vascular disorders/ Peripheral artery occlusion/ OCCLUSION OF ARTERIA FEMORALIS SUPERFICIALIS	S: 11OCT2018 (988) E:	AESI	C: 3, 7 D: 21DEC2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 21DEC2018 (1059) E:	AESI	C: 1, 2, 3, 7 D: 21DEC2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Arterial bypass occlusion/ ACUTE BYPASS OCCLUSION	S: 15JAN2017 (393) E: 17JAN2017 (395)	AESI	C: 3, 7 D: 29OCT2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Injury, poisoning and procedural complications/ Vascular graft occlusion/ SUSPICION OF CRITICAL ISCHEMIA CAUSED BY BYPASS OCCLUSION	S: 27OCT2017 (678) E: 27OCT2017 (678)	AESI	C: 3, 7 D: 29OCT2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ ARTERIO-VENOUS SHUNT OCCLUSION	S: 24NOV2017 (706) E: 25NOV2017 (707)	AESI	C: 3, 7 D: 29OCT2018	RECOVERED/ RESOLVED	DRUG WITHDRAWN		NOT RELATED
Injury, poisoning and procedural complications/ Arterial bypass occlusion/ ACUTE FEMOROPOPLITEAL ARTERY BYPASS OCCLUSION	S: 20APR2018 (853) E: 30APR2018 (863)	AESI	C: 3, 7 D: 29OCT2018	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF DRUG EFFECT	S: 29MAY2017 (522) E:	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 19OCT2016 (279) E: 26OCT2016 (286)	AESI	C: 3, 7 D: 28APR2018	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE STAGE IV	S: 12MAR2018 (777) E:	AESI	C: 1, 2, 3, 7 D: 12MAR2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 22NOV2017 (715) E:	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18SEP2017 (645) E: 19SEP2017 (646)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 25APR2018 (821) E:	AESI	C: 1, 2, 3, 7 D: 25APR2018	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 21SEP2018 (986) E: 26SEP2018 (991)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION OF LEFT FOREARM WITH SHUNT INFECTION	S: 31OCT2018 (1026) E: 05NOV2018 (1031)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DRUG WITHDRAWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHEMIC ATTACK	S: 19JUL2016 (71) E: 10AUG2016 (93)	AESI	C: 6, 7 D: 08FEB2017	RECOVERED/ RESOLVED	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 06NOV2017 (669) E:	AESI	C: 1, 3, 7 D: 06NOV2017	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Investigations/ Haemoglobin decreased/ HEMOGLOBIN DECREASE	S: 05MAR2016 (54) E:	ADR	C: 1, 2, 7 D: 09MAR2016	FATAL	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 14JUL2016 (21) E:	AESI	C: 1, 2, 3, 7 D: 14JUL2016	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Intestinal infarction/ MESENTERIC INFARCTION	S: 13JAN2017 (61) E:	AESI	C: 1, 2, 3, 7 D: 13JAN2017	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Carotid artery restenosis/ CAROTIS STENOSIS	S: 26SEP2018 (857) E:	AESI	C: 1, 2, 3, 7 D: 26SEP2018	FATAL	NOT APPLICABLE		UNLIKELY RELATED
Nervous system disorders/ Ischaemic stroke/ LEFT HEMISPHERIC ISCHEMIA AT CAROTIS STENOSIS	S: 26SEP2018 (857) E:	AESI	C: 1, 2, 3, 7 D: 26SEP2018	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Product issues/ Thrombosis in device/ CATHETER ASSOCIATED THROMBUS IN VENA CAVA SUPERIOR	S: 03DEC2018 (937) E: 25JAN2019 (990)	AESI	C: 3, 7 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 21JUN2018 (760) E:	AESI	C: 3, 7 D:	NOT RECOVERED/NOT RESOLVED	UNKNOWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 24AUG2017 (366) E:	AESI	C: 2, 3, 5, 7 D: 18OCT2018	NOT RECOVERED/NOT RESOLVED	DRUG WITHDRAWN		UNLIKELY RELATED
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18JUL2018 (694) E: 13SEP2018 (751)	AESI	C: 2, 3, 5, 7 D: 18OCT2018	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ NEWLY DIAGNOSED PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 21JAN2019 (206) E:	AESI	C: 3, 5, 7 D: 21DEC2019	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 03AUG2016 (87) E: 03AUG2016 (87)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE REDUCED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral artery occlusion/ OCCLUSION OF ARTERIA CEREBRI MEDIA LEFT WITH HEMIPARESIS RIGHT.	S: 02DEC2019 (910) E: 03DEC2019 (911)	AESI	C: 2, 3, 7 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		POSSIBLE RELATED
Nervous system disorders/ Hemiparesis/ OCCLUSION OF ARTERIA CEREBRI MEDIA LEFT WITH HEMIPARESIS RIGHT.	S: 02DEC2019 (910) E: 03DEC2019 (911)	AESI	C: 2, 3, 7 D:	RECOVERING/ RESOLVING	DOSE NOT CHANGED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 26SEP2018 (860) E: 30SEP2018 (864)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE INCREASED		UNLIKELY RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 26SEP2018 (860) E: 30SEP2018 (864)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 25FEB2019 (1012) E: 26FEB2019 (1013)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	DOSE INCREASED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Therapeutic product effect decreased/ DECREASED EFFECT	S: 21OCT2017 (523) E:	AESI	C: 2, 7 D:	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: APR2017 E:	AESI	C: 1, 2, 3, 7 D: 18APR2017	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	C: 1, 2, 3, 7 D: 06SEP2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	C: 1, 2, 3, 7 D: 06SEP2017	FATAL	UNKNOWN		UNKNOWN
Nervous system disorders/ Cerebral haemorrhage/ HEMORRHAGE INTRACEREBRAL	S: 06SEP2017 (70) E:	AESI	C: 1, 2, 3, 7 D: 06SEP2017	FATAL	UNKNOWN		UNKNOWN

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INADEQUATE HEMOGLOBIN INCREASE, HYPERREGENERATIVE ANEMIA, HAEMORRHAIGIC ANEMIA (LACK OF DRUG EFFECT).	S: E:	AESI	C: 6, 7 D: 09FEB2020	UNKNOWN	DRUG WITHDRAWN		NOT RELATED
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 09FEB2020 (956) E:	AESI	C: 1, 2, 3, 7 D: 09FEB2020	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 26OCT2017 (256) E:	AESI	C: 1, 2, 3, 7 D: 26OCT2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHAEMIC STROKE	S: 14MAR2019 (804) E: 30MAR2019 (820)	AESI	C: 2, 3, 7 D:	RECOVERED/ RESOLVED	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 07DEC2017 (297) E:	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebrovascular accident/ UNSPECIFIED STROKE	S: 07APR2019 (187) E:	AESI	C: 1, 2, 3, 7 D: 07APR2019	FATAL	NOT APPLICABLE		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 08FEB2018 (360) E:	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 11MAR2019 (438) E:	AESI	C: 1, 2, 7 D: 11MAR2019	FATAL	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 20NOV2017 (223) E:	AESI	C: 1, 2, 3, 7 D: 20NOV2017	FATAL	DRUG WITHDRAWN		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 29APR2019 (185) E: 03MAY2019 (189)	AESI	C: 3, 7 D: 09APR2020	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Deep vein thrombosis/ DEEP VEIN THROMBOSIS FEMORAL	S: 25APR2019 (127) E:	AESI	C: 1, 3, 7 D: 25APR2019	UNKNOWN	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 18MAY2019 (167) E: 21MAY2019 (170)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: 01FEB2019 (232) E: 08FEB2019 (239)	AESI	C: 3, 7 D: 11MAR2019	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TRANSIENT ISCHAEMIC ATTACK	S: 18APR2019 (338) E: 20APR2019 (340)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Ischaemic stroke/ ISCHEMIC STROKE	S: 19FEB2019 (299) E: 18MAR2019 (326)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Cardiac disorders/ Myocardial infarction/ MYOCARDIAL INFARCTION	S: MAR2019 E: 04APR2019 (88)	AESI	C: 3, 7 D: 01NOV2019	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

De-117-B016/C/M
Treatment Group: SILAPO

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 19MAR2019 (285) E: 23MAR2019 (289)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED
Injury, poisoning and procedural complications/ Shunt thrombosis/ SHUNT THROMBOSIS	S: 30MAR2019 (296) E: 08APR2019 (305)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ INADEQUATE LOW HAEMOGLOBIN CONCENTRATION (LACK OF DRUG EFFECT)	S: 18SEP2019 (150) E:	AESI	C: 6, 7 D:	RECOVERING/ RESOLVING	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Arterial thrombosis/ ARTERIAL THROMBOSIS	S: 20DEC2019 (432) E: 27DEC2019 (439)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED
Vascular disorders/ Peripheral arterial occlusive disease/ PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	S: 20DEC2019 (432) E: 27DEC2019 (439)	AESI	C: 3, 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Thrombophlebitis superficial/ THROMBOPHLEBITIS OF LEFT LOWER LEG (SUPERFICIAL VEIN, NO DEEP LEG VEIN THROMBOSIS)	S: 15MAR2019 (159) E: 22APR2019 (197)	AESI	C: 5, 7 D:	RECOVERED/ RESOLVED WITH SEQUELAE	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ SHUNT OCCLUSION	S: 21OCT2019 (351) E: 23OCT2019 (353)	AESI	C: 3, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Subclavian vein thrombosis/ SUBCLAVIAN VEIN THROMBOSIS RIGHT	S: 29DEC2019 (423) E: 21FEB2020 (477)	AESI	C: 6, 7 D:	RECOVERED/ RESOLVED	DOSE NOT CHANGED		UNLIKELY RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	C: Criteria[a] D: Death Date	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Injury, poisoning and procedural complications/ Shunt occlusion/ RELAPSE OF THROMBOTIC SHUNT OCCLUSION	S: 11FEB2019 (88) E:	AESI	C: 3, 7 D: 31JUL2019	NOT RECOVERED/NOT RESOLVED	DOSE NOT CHANGED		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; SAE=Serious Adverse Event; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:37)

Es-024-0023/74/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Dermatitis allergic/ SKIN ALLERGIC	S: 13FEB2013 (1) E:	ADR	RECOVERING/ RESOLVING		TEMPORARILY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Dizziness/ DIZZINESS	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Nervous system disorders/ Headache/ HEADACHE	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Vascular disorders/ Hypertension/ HYPERTENSION	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
General disorders and administration site conditions/ Malaise/ MALAISE	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Gastrointestinal disorders/ Nausea/ NAUSEA	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Cardiac disorders/ Palpitations/ PALIPITATION	S: 26JUL2012 (1) E: 28JUL2012 (3)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED

Ge-048-0008/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Malaise/ INDISPOSITION	S: DEC2012 E: JAN2013	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Psychiatric disorders/ Nightmare/ NIGHTMARE	S: DEC2012 E: JAN2013	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-048-0016/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Vascular disorders/ Embolism/ THROMBOEMBOLIC EVENTS	S: E:	AESI	UNKNOWN	UNKNOWN		N/A

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-067-0018/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Reproductive system and breast disorders/ Breast disorder/ SENSATION OF TENSION IN HER BREAST	S: 03AUG2012 (52) E:	ADR	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Cerebral infarction/ PONS INFARCT	S: 24JUL2012 (272) E: 14AUG2012 (293)	AESI	RECOVERED/ RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-097-0007/48/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: E:	AESI	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-097-0016/50/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: E:	AESI	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-101-0001/81/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Headache/ HEADACHE	S: 07MAR2012 (128) E:	ADR	RECOVERED/ RESOLVED		NO DATA	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-142-0006/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Lip swelling/ SWELLING OF LIPS	S: 26APR2011 (15) E: 27APR2011 (16)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Gastrointestinal disorders/ Swollen tongue/ SWELLING OF TONGUE	S: 26APR2011 (15) E: 27APR2011 (16)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Reproductive system and breast disorders/ Vulvovaginal pruritus/ PRURITUS OF VAGINA	S: 26APR2011 (15) E: 27APR2011 (16)	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-147-0001/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Pruritus/ PRURITUS	S: E:	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED
Skin and subcutaneous tissue disorders/ Rash/ RED EFFLORESCENCES ON THE SKIN	S: E:	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-463-0008/C/F
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 22MAY2013 (83) E: 01JUL2014 (488)	AESI	UNKNOWN		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Ge-479-0001/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Malaise/ FEELING UNWELL	S: E:	ADR	UNKNOWN	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Headache/ HEADACHE	S: 13AUG2013 (62) E:	ADR	UNKNOWN		PERMANENTLY WITHDRAWN	NOT RELATED
Skin and subcutaneous tissue disorders/ Pruritus/ ITCHING	S: 13AUG2013 (62) E:	ADR	UNKNOWN		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: E:	AESI	UNKNOWN	UNKNOWN		RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Transient ischaemic attack/ TIA	S: 10NOV2016 (519) E:	AESI	RECOVERED/ RESOLVED	NOT APPLICABLE		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 04MAR2012 (21) E:	AESI	NOT RECOVERED/NOT RESOLVED		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Sw-005-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 20APR2012 (68) E:	AESI	NOT RECOVERED/NOT RESOLVED		PERMANENTLY WITHDRAWN	NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 24MAY2012 (95) E:	AESI	NOT RECOVERED/NOT RESOLVED	UNKNOWN		NOT RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
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System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Drug ineffective/ LACK OF EFFICACY	S: 01MAR2012 (14) E:	AESI	NOT RECOVERED/NOT RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

Sw-018-0010/C/M
Treatment Group: RETACRIT

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
General disorders and administration site conditions/ Influenza like illness/ INFLUENZA LIKE SYMPTOMS	S: E:	ADR	RECOVERED/ RESOLVED		PERMANENTLY WITHDRAWN	RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Pruritus/ PRURITUS	S: APR2011 E: FEB2012	ADR	RECOVERED/ RESOLVED	UNKNOWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Nervous system disorders/ Dyskinesia/ INVOLUNTARY FACE TICS	S: 06SEP2013 (689) E: 11NOV2013 (755)	ADR	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Eczema/ SEVERE ITCHING ECZEMA OF HANDS, LEGS, KNEES AND TIGHS	S: 03DEC2012 (288) E: 08MAY2013 (444)	ADR	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Dermatitis allergic/ ALLERGIC EXANTHEMA ON ARMS AND LEGS	S: E:	ADR	UNKNOWN	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Musculoskeletal and connective tissue disorders/ Bone pain/ BONE PAIN	S: 23NOV2015 (896) E: 23NOV2015 (896)	ADR	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Skin and subcutaneous tissue disorders/ Hypertrichosis/ HYPERTRICHOSIS	S: SEP2013 E: 15NOV2013 (99)	ADR	RECOVERED/ RESOLVED	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

System Organ Class/ Preferred Term/ Investigator Entry	S: Start Date (Study Day) E: End Date (Study Day)	AESI/ ADR	Outcome	Action Taken with Study Drug	Other Action Taken	Related to Study Drug
Gastrointestinal disorders/ Nausea/ NAUSEA	S: E:	ADR	UNKNOWN	DRUG WITHDRAWN		POSSIBLE RELATED
Gastrointestinal disorders/ Vomiting/ VOMITING	S: E:	ADR	UNKNOWN	DRUG WITHDRAWN		POSSIBLE RELATED

[a] Criteria: 1 = Death, 2 = Life-threatening, 3 = Requires or Prolongs Hospitalization, 4 = Congenital Anomaly, 5 = Persistent or Significant Disability/Incapacity, 6 = Important Medical Event Requiring Medical or Surgical Intervention, 7 = Concomitant or Additional Treatment Given
Note: The listing only includes protocol-specified AESI or ADR that are Treatment Emergent: event started after the start of Epoetin Zeta treatment until the end of the observation period for the study. The adverse drug reactions (ADR) will consist of all treatment-related adverse events but not considered as AESI. Adverse Events: total of AESI and ADR.
AESI=Adverse Event of Special Interest; ADR=Adverse Drug Reaction
MedDRA v23.0 coding dictionary was applied.
PFIZER CONFIDENTIAL Source Data: Appendix 7.7 Date of Table Generation: 12AUG2020 (17:39)

TABLE OF CONTENTS

15.3.12.1 Death Narratives

Narratives are provided for only study protocol defined adverse events of special interest or treatment related event (adverse drug reaction) resulting in death are listed below:

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
Bg-001-0024	2574411	Myocardial infarction
Bg-001-0048	2016495673	Ischaemic stroke
Bg-004-0004	2400201	Ischaemic stroke
Bg-004-0041	2016403477	Myocardial infarction
Bg-004-0094	2018473550	Myocardial infarction
Bg-006-0039	2017489626	Cerebrovascular accident
Bg-014-0002	2085987	Acute myocardial infarction; Pulmonary embolism
Bg-014-0003	2939556	Myocardial infarction
Bg-014-0004	2327613	Ischaemic stroke
Bg-015-0017	3181623	Cerebrovascular accident
Bg-025-0011	2017495875	Myocardial infarction
Cr-005-0002	2017098040	Myocardial infarction
Cr-005-0014	2016267631	Subdural haematoma
Es-024-0025	2999144	Acute myocardial infarction
Es-024-0038	2017447054	Acute myocardial infarction
Fin-001-0002	3137952	Myocardial infarction
Fr-064-0019	1685920	Cerebrovascular accident
Ge-012-0007	892943	Cerebrovascular accident
Ge-012-0017	1891763	Cerebrovascular accident
Ge-012-0022	1891768	Thrombosis in device
Ge-027-0028	1897663	Myocardial infarction
Ge-048-0041	2018308638	Cerebral haemorrhage
Ge-069-0010	2018371800	Infarction
Ge-083-0006	1793228	Pulmonary embolism
Ge-083-0008	2400258	Cerebrovascular accident
Ge-093-0085	2400091	Cerebral infarction; Cerebral ischaemia
Ge-094-0032	2017435221	Myocardial infarction
Ge-109-0003	2820900	Acute myocardial infarction
Ge-115-0015	998219	Arterial thrombosis
Ge-146-0003	2052813	Acute myocardial infarction
Ge-152-0025	2651469	Myocardial infarction
Ge-454-0018	2817079	Myocardial infarction
Ge-463-0008	2021971	Subdural haematoma; Basal ganglia haemorrhage
Ge-463-0015	2233652	Myocardial infarction
Ge-471-0015	2715463	Pulmonary embolism
Ge-471-0016	2016459865	Myocardial infarction
Ge-471-0033	2016583774	Myocardial infarction
Gr-002-0019	2693195	Acute myocardial infarction

Gr-002-0025	2797025	Myocardial infarction
Gr-003-0012	2453067	Myocardial infarction
Gr-013-0002	2016295847	Acute myocardial infarction
Gr-031-0004	2411460	Myocardial infarction
Gr-034-0009	2017358130	Myocardial infarction
Gr-034-0010	2017358127	Cerebrovascular accident
Gr-045-0026	2737056	Pulmonary embolism
Gr-045-0051	2018212348	Myocardial infarction
Gr-051-0005	2602755	Myocardial infarction
Gr-051-0024	3084735	Embolism
Gr-051-0031	2605484	Myocardial infarction
Gr-051-0085	2017253323	Myocardial infarction
Gr-051-0090	2017244407	Myocardial infarction
Gr-052-0006	2965870	Cerebrovascular accident
Gr-052-0010	3168514	Cerebral haemorrhage
Gr-059-0006	2018036059	Myocardial infarction
Gr-062-0006	3073610	Cerebrovascular accident
Gr-065-0005	3272375	Myocardial infarction
It-038-0014	1391691	Haemorrhagic stroke
It-090-0022	2791899	Cerebral haemorrhage
It-093-0005	2069922	Cerebrovascular accident
It-116-0018	2016281626	Myocardial infarction
It-116-0021	2649763	Acute myocardial infarction
It-116-0024	2789600	Cerebrovascular disorder
It-120-0019	2653522	Cerebrovascular accident
It-120-0033	2018006285	Acute myocardial infarction
Sw-005-0002	2139224	Myocardial infarction
Sw-005-0014	2188609	Myocardial infarction
Sw-005-0039	3291130	Acute myocardial infarction
Sw-011-0023	2016443936	Myocardial infarction
Sw-011-0028	2018182041	Cerebral haemorrhage
Sw-018-0003	1550791	Myocardial infarction
Sw-018-0008	2819992	Myocardial infarction

This clinical trial report contains narratives printed in a CIOMS format with a “Draft” watermark. This watermark signifies that these narratives were not produced for the submission of individual case safety reports to a regulatory agency. These narratives contain the information available in the safety database as of 27-Aug-2020 and are considered final.

DEATH NARRATIVE

Patient ID Number: Ge-069-0010

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2960188, 2018371800

The following narrative criteria were met:

- Death
- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Cerebrovascular accident (AER# 2960188)	Stroke
Infarction (AER# 2018371800)	Second infarct
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Cause of Death:	
Infarction	Second infarct

This 56-year-old White male patient was enrolled in post-authorization safety cohort observation study on 01 Oct 2014 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of type 2 diabetes mellitus, hypertension, end stage renal disease, coronary artery disease, diabetic nephropathy, cerebrovascular insufficiency, and cerebrovascular accident (all since unknown dates); prostate cancer (diagnosed in 1999); and renal failure (since 08 Oct 2013). The patient was an ex-smoker.

The patient was not on dialysis, and he received prior SC epoetin zeta from 29 Sep 2014 and started receiving SC epoetin zeta at a total dosage of 60 IU/kg/week (1 dosage/week) from 01 Oct 2014 (Study Day 1). Concomitant medications included bisoprolol, insulin glargine, clopidogrel, and citalopram.

On 13 Mar 2015 (Study Day 164), the patient had a reported event of stroke (MedDRA preferred term [PT]: cerebrovascular accident). He was hospitalized on an unspecified date due to cerebrovascular accident. The details on the laboratory/diagnostic tests performed and the treatment given were not reported. The action taken with epoetin zeta in response to the event and the event outcome were reported as unknown. On an unknown date, the patient was discharged from the hospital.

The patient completed the study on 25 Sep 2017 (Study Day 1091).

On 18 Oct 2018 (Study Day 1479), after one year of the completion of the study, the patient had a reported event of second infarct (MedDRA PT: infarction). The patient died on the same day (Study Day 1479) due to cerebral hemorrhage. The action taken with epoetin zeta in response to the event was not applicable. No autopsy was performed.

The Investigator's causality for the event of cerebrovascular accident and epoetin zeta was not reported. The Sponsor assessed that there was a reasonable possibility that the event of cerebrovascular accident was related to epoetin zeta based on medical plausibility. The Sponsor also stated that epoetin zeta could increase the risk of thromboembolic events by increasing red cell concentration; however, the contributory effects of other cardiovascular risk factors such as hypertension, diabetes and previous smoking history should also be considered.

The Investigator's causality for the event of infarction and epoetin zeta was reported as not applicable. The Sponsor assessed that there was not a reasonable possibility that the event of infarction was related to epoetin zeta, given the event occurred more than one year after the discontinuation of epoetin zeta and the patient's medical history of type 2 diabetes mellitus, end stage renal disease, coronary artery disease, and cerebrovascular insufficiency.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

DEATH NARRATIVE

Patient ID Number: Sw-005-0002

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 1402439, 2139224

The following narrative criteria were met:

- Death
- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Myocardial infarction (AER# 1402439)	Myocardial infarction
Myocardial infarction (AER# 2139224)	Myocardial infarction
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Cause of Death:	
Myocardial infarction (AER# 2139224)	Myocardial infarction

This 52-year-old White male patient was enrolled in post-authorization safety cohort observation study on 13 Feb 2012 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of renal failure (since 23 Apr 1998); diabetic nephropathy, cerebrovascular disorder, coronary artery disease, type 1 diabetes mellitus, hypertension, myocardial infarction, hyperlipidemia, peripheral arterial occlusive disease, embolism, transient ischemic attack, myocardial ischemia, and cerebrovascular accident (all since unknown dates).

The patient began dialysis 3 times per week from 18 Aug 2004, and he received prior Eprex 73 IU/kg/week from 10 Jun 2002 to 03 Oct 2011, and SC epoetin zeta 4000 IU, 2 times a week from 04 Oct 2011. The patient started receiving SC epoetin zeta at a total dosage of 138 IU/kg/week (2 dosage/week) from 13 Feb 2012 (Study Day 1). It was reported that the patient experienced four thromboembolic events (all acute myocardial infarctions) during treatment with Eprex. No concomitant medications were reported.

On 21 Mar 2012 (Study Day 38), two days after receiving a dose of epoetin zeta, the patient experienced a reported event of myocardial infarction (MedDRA preferred term [PT]: myocardial infarction-first occurrence) due to fluid overload. The event of myocardial infarction was a life-threatening event. The patient underwent dialysis as treatment to reduce the fluid overload. On the same day (Study Day 38), the patient's laboratory investigations showed platelet count at 186 × 10^9/L (normal range [NR]: 140-350× 10^9/L), sodium at 140 mmol/L (NR: 137-145 mmol/L), potassium at 3.3 mmol/L (NR: 3.5-4.4 mmol/L), N-terminal prohormone brain natriuretic peptide at >35000 ng/L (NR: <900 ng/L; grey zone at 300-900 ng/L), C-reactive protein at 98 mg/L (NR: <10 mg/L), and creatinine at 349 µmol/L (NR: 60-105 µmol/L). The action taken with epoetin zeta in response to the event of myocardial infarction (first occurrence) was not reported. On 30 Mar 2012 (Study Day 47), the event of myocardial infarction (first occurrence) resolved.

On 06 Jan 2014 (Study Day 694), the patient received a dose of epoetin zeta. On the same day (Study Day 694), the patient was admitted to the hospital due to sepsis. On 09 Jan 2014 (Study Day 697), three days after receiving a dose of epoetin zeta, the patient experienced a reported event of myocardial infarction (MedDRA PT: myocardial infarction-second occurrence), which was a life-threatening event. On the next day (Study Day 698), the patient's troponin T was 446 ng/L (NR: <15 ng/L). An electrocardiogram (ECG) showed ventricular rate of 111 beats per minute, PQ time of 196 msec, QRS duration of 114 msec, QT/QTc of 312/424 msec, and PR-T axis of 77 -2 146. The ECG indicated sinus tachycardia, suspected pathological delayed atrioventricular conduction, unspecified intraventricular conduction defect, ST depression, predominant ischemia, and ANT-LAT aVL. The action taken with epoetin zeta in response to the event of myocardial infarction (second occurrence) was reported as not applicable. The patient received palliative treatment for the event (details not available). On 11 Jan 2014 (Study Day 699), the patient died due to myocardial infarction subsequent to septicemia. It was not reported if an autopsy was performed.

In the opinion of the Investigator, there was not a reasonable possibility that the events of myocardial infarction were related to epoetin zeta. The Sponsor concurred with this assessment that the reported events of acute myocardial infarction were not related to epoetin zeta. According to the Sponsor, the first event of myocardial infarction was due to underlying medical condition given the multiple cardiac risk factors in the medical history; and the second event of myocardial infarction was noted to be secondary to septicemia.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

DEATH NARRATIVE

Patient ID Number: Sw-011-0028

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2018213835, 2018182041

The following narrative criteria were met:

- Death
- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Cerebrovascular accident (AER# 2018213835)	Stroke
Cerebral haemorrhage (AER# 2018182041)	Intracerebral hemorrhage
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	
Cerebral haemorrhage	Intracerebral hemorrhage

This 63-year-old White male patient was enrolled in post-authorization safety cohort observation study on 25 Mar 2015 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of glomerulonephritis, pain in extremity, anemia, and osteoporosis (all since unknown dates); renal failure (since 1996); hypertension (since 2009); peripheral arterial occlusive disease (since 2014); and hyperparathyroidism (since 13 Feb 2015). The patient was an ex-smoker.

The patient was on peritoneal dialysis from 02 Jul 2015 (Study Day 100), and he started receiving SC epoetin zeta at a total dosage of 93.75 IU/kg/week (1 dosage/week) from 13 Mar 2015. Concomitant medications included capsaicin, dimeticone, alfacalcidol, furosemide, pregabalin, ondansetron, sodium polystyrene sulfonate, naloxone hydrochloride/oxycodone hydrochloride, omeprazole, candesartan cilexetil, sevelamer carbonate, acetylsalicylic acid, iodixanol, macrogol/potassium chloride/sodium bicarbonate/sodium chloride, magnesium citrate/magnesium lactate, paracetamol, benserazide hydrochloride/levodopa, pramipexole dihydrochloride, calcitonin/salmon, lactulose, simvastatin, sodium citrate acid/taurolidine, Venofer, sodium picosulfate, oxycodone hydrochloride, piperacillin sodium/tazobactam sodium, ertapenem sodium, and erythrocytes.

On 02 Nov 2017 (Study Day 954), the patient was hospitalized due to the left sided hemiparesis, neglect, and dysarthria. The patient was diagnosed with a reported event of stroke (MedDRA preferred term [PT]: cerebrovascular accident), which was a life-threatening event resulting in hospitalization. A computerized tomogram (CT) on an unspecified date showed no clear infarction of recent origin, and a CT of the neck on 02 Nov 2017 (Study Day 954) showed no signs of thrombus. On the same day, the patient's diastolic blood pressure (BP) ranged between 94 mmHg and 135 mmHg and a systolic BP ranged between 146 mmHg and 216 mmHg; pulse rate was 104 beats/minute,

and a C-reactive protein (CRP) was 26 mg/L and 21 mg/L (normal range [NR]: <3 mg/L). The patient was switched to hemodialysis, as he could not take care of his peritoneal dialysis. No action taken with epoetin zeta in response to the event. However, epoetin zeta was discontinued on 01 Dec 2017 (Study Day 983) and changed to darbepoetin alfa (Aranesp) per department policy as the patient began hemodialysis. No treatment information was reported. On 07 Dec 2017 (Study Day 989), the patient was discharged from the hospital. On an unknown date, the patient recovered from the event with sequelae of decreased strength in left arm, slight dysarthria, neglect of left side, difficult to move, and unable walk due to decreased strength in the left leg.

It was reported that the patient recently experienced septicemia from 27 Dec 2017 (Study Day 1009) to 04 Jan 2018 (Study Day 1017).

On 06 Jan 2018 (Study Day 1019), the patient had a severe headache and loss of consciousness, and he was admitted to the hospital. On the same day, a CT showed a massive right-side hemorrhage in the brain. The patient was diagnosed with a reported event of intracerebral hemorrhage (MedDRA PT: cerebral hemorrhage), which was life-threatening and caused persistent or significant disability/incapacity. The patient's diastolic BP readings were 118, 111, and 100 mmHg and systolic BP readings were 222, 170, and 200 mmHg. The patient's CRP was 13 mg/L and white blood cell (WBC) count of 22.2×10^9/L (NR: $3.5\text{-}8.8 \times 10^9$/L). On 06 Jan 2018 (Study Day 1019), the patient was treated with calcium chloride dehydrate/ magnesium chloride hexahydrate/ potassium chloride/sodium acetate/ sodium chloride. On 07 Jan 2018 (Study Day 1020), a CT showed a massive right-side parenchymal hemorrhage (approximately 8.5 cm). A CT thorax showed a small amount of pleural fluid bilaterally and a chest x-ray showed no infiltration or pleural fluid. On the same day, the patient's CRP was 25 mg/L and WBC count was 24.9×10^9/L. The patient died on the same day (Study Day 1020) due to the event of cerebral hemorrhage. It was reported that 'like all patients with stage 5 chronic kidney disease', the patient had homocysteinemia as a risk factor for thromboembolic events; however, no measurements were provided. It was also reported that acetylsalicylic acid, and tinzaparin sodium were permanently discontinued as a result of event on an unspecified date.

In the opinion of the Investigator, there was not a reasonable possibility that the event of cerebrovascular accident was related to epoetin zeta or to any concomitant medication. The Sponsor did not concur with this assessment and reported that the event of cerebrovascular accident was related to epoetin zeta.

In the opinion of the Investigator, there was not a reasonable possibility that the event of cerebral haemorrhage was related to epoetin zeta, but related to acetylsalicylic acid. The Sponsor concurred with this assessment that the reported event of cerebral haemorrhage was not related to epoetin zeta. According to the Sponsor, the event of cerebral haemorrhage was most likely related to an intercurrent or underlying condition.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GERMANY	01	APR	1937	73 Years	Male	113.00 kg	06	APR	2011

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplexy [Cerebrovascular accident]

Case Description: PASCO ll : this is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO ll) describing a fatal case of apoplexy with Retacrit, from Germany. Patient
number Ge-012-0007. This spontaneous report from Germany describes a 73 year old male patient who received treatment with Retacrit (epoetin zeta; administered twice a week, mean dose of 6000 IE per week, subcutaneous; lot number

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 07-APR-2011
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IE, Freq: 2 week, Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 05-NOV-2010 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FALITHROM (PHENPROCOUMON) ; 26-MAY-2004 / Unknown
#2) ALLOPURINOL (ALLOPURINOL) ; 02-JUL-2004 / Unknown
#3) DIGITOXIN (DIGITOXIN) ; 24-JAN-2009 / Unknown
#4) FUROSEMIDE (FUROSEMIDE) ; 07-MAY-2010 / Unknown
#5) METOPROLOL (METOPROLOL) ; 02-JUL-2004 / Unknown
#6) RAMIPRIL (RAMIPRIL) ; 07-MAY-2010 / Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History 1997	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
892943

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-APR-2011

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 892943

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

not reported) initiated on 05-Nov-2010 for renal anaemia. The patient's medical history included hyperlipidemia (since 2004), ischaemic heart disease (stage I, since 2004), diabetes mellitus (since 2000), atrial fibrillation (since 1997), and coronary heart disease (since 1997). Concomitant medication included ramipril and metoprolol for hypertension, digitoxin and falithrom for thoracic aortic aneurysm (TAA), allopurinol for hyperuricemia, and xipamide and furosemide for chronic renal failure (CRF). On 05-Nov-2010 the patient initiated treatment with Retacrit. On 06-Apr-2011, the patient experienced apoplexy, and died on 07-Apr-2011. Reason for death was reported as apoplexy. At the time of the report, an autopsy had not been performed. No further information was reported. The reporting Physician considered the relationship between treatment with Retacrit and the death due to apoplexy as not assessable. 08-Mar-2013: Corrected report. Report source was changed to post marketed study (previously reported as health professional). Proprietary Medicinal Product names of Epoetin zeta and Falithrom were selected. Time from first dose to onset of epoetin zeta was populated in the structured field. Apoplexy was structured under patient death cause section. Data entry corrections were also made in patient's medical history, frequency of suspect drug, and in the narrative to reflect patient's height and weight. Patient's weight was 113 kg and height was 196 cm. The patient did not have any exposure to other erythropoetin-stimulatig agent (ESA). Frequency of epoetin zeta was populated under dosage fields (number of separate dosages, interval number and definition of interval). The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit (epoetin zeta): Batch number and date of expiry. 26-Apr-2013: Corrected report was created to correct the study name in the study name field.

Case Comment: Overall Case Causality: Not Assessable While seemingly temporally related and noting reporter assessment as not assessable, unable to evaluate event for causation without further objective clinical event details and an autopsy report if any Follow-up (23 March 2013): Data entry corrections do not warrant change in previous causality assessment. - N. Gonzales (23 March 2013) Follow-up (03 May 2013): Correction to case does not warrant change in previous causality assessment. - N. Gonzales (03 May 2013)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) XIPAMIDE (XIPAMIDE) ; 07-MAY-2010 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, and alcohol, consumption were not reported. The patient did not smoke. 08-Mar-2013: Data entry correction was also made to reflect that the patient did not have any previous exposure to other erythropoietinstimulating agent (ESA). On 07-Apr-2011, the patient died. Reason for death was reported as apoplexy. At the time of the report, an autopsy had not been performed.
Unknown to Ongoing	Relevant Med History 1997	Coronary heart disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History 2000	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History 2004	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History Stage I, 2004	Ischemic heart disease (Myocardial ischaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	16	NOV	1941	69 Years	Male	74.00 kg	14	MAR	2011	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Arterial thrombosis [Arterial thrombosis]

Case Description: This is a Hospira-Sponsored Post authorisation safety cohort observation (PASCO) of retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal arterial
thrombosis. This case describes a 69-year-old Caucasian male patient (1150015) who received epoetin zeta (68 IE/Kg, subcutaneous, once a week; batch number and formulation not reported) for renal anemia starting on 21-Feb-2011.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 22-MAR-2011
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 68 IU/kg, (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-FEB-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Arteriosclerosis (Arteriosclerosis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
998219

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-AUG-2011

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included surgery with Gore Tex prosthesis leg on Dec-2010, vascular anomalies described as AVK of leg, aneurysm spurium after vascular partition. Concurrent diseases included peripheral arterial disease and hypertension.
Patient is a smoker. The patient has never had treatment with any erythropoiesis-stimulating agent (ESA) prior to enrolment to PASCO II. The patient did not undergo dialysis and had no concurrent medications. On 21-Feb-2011, the patient began epoetin zeta. On 14-Mar-2011, the patient experienced arterial thrombosis of artery of pelvis and legs, due to arteriosklerosis. On 18-Mar-2011, the patient had an operation. On 19-Mar-2011 the patient had reoperation, which showed the thrombosis. The outcome of the event was fatal. The action taken with epoetin zeta was unknown. The patient died on 22-Mar-2011. Cause of death was sepsis and multi organ failure. It was not reported if an autopsy was done. No further information provided. The reporter's causality assessment for the event of fatal arterial thrombosis in relation to epoetin zeta therapy was not related. English translation of the letter from the hospital's assistant medical director received on 08-Aug-2011. Additional information was obtained regarding the patient's medical history and the events. Medical history included membranous glomerulonephritis diagnosed as early as 1998; lacunar medial cerebral artery infarct in 2007; chronic infection of an aortic right iliac/left femoral bifrcation prosthesis (Y-prostheses) implanted in 2004; above-the-knee amputations on the right in 2010; prosthesis to deep femoral artery vascular prosthesis implant on Dec-2010; obstructive arterial peripheral vascular disease treated at another institution with extensive surgery, with placement of a femoral-popliteal prosthetic bypass on the right and placement of an aortic-right iliac/left femoral bifurcation prosthesis (Y-prosthesis), and left false femoral aneurysm demostrated along with severe arteriosclerosis. From 13-Dec to 28-Dec-2010, there next followed a vascular surgical operative intervention after the patient was admitted to the hospital on an emergency basis with progressive obstructive peripheral arterial disease and progression to stage III in the area of the left leg. On 18-March-2011, there followed the operative intervention for explantation of the bifurcation prosthesis (Y-prosthesis). On 19-Mar-2011, the first post-operative day, a renewed operation was required, the patient had transfemoral thrombectomy and placement of an extra-anatomical right axillary-right femoral bypass. On the second post-operative day, progressive cardiovascular failure occurred during renal replacement therapy so that on 20 March 2011, another laparotomy was required for hemostasis and to relieve a pronounced abdominal compartment syndrome.
On an unspecified date, despite comprehensive intensive medical and surgical efforts, progressive vascular supply disturbances occurred in the area of the left lower leg, the amputation stump on the right, as well as the gluteal soft tisues with a lethal outcome. It was stated the advanced state of the patient's illness no longer permitted a favorable outcome.

Case Comment: Overall Case Causality: Not Related Agree with reporter causality; consider event more likely due to progression of pre-existent medical conditions and past medical history Overall Case Causality (Follow-up 17 Aug 2011): Not Related - edits to case do not change assessment No Change

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body height	175 CM	
2		Weight	74 kg	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	68 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	21-FEB-2011 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Patient is a smoker. Alleriges and alcohol consumption were not reported. Patient died on 22-Mar-2011. Cause of death was sepsis and multi organ failure. It was not reported if an autopsy was done.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Glomerulonephritis membranous (Glomerulonephritis membranous); diagnosed as early as 1998

Mfr. Control Number: 998219

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History 2010	Above knee amputation (Leg amputation);
Unknown	Relevant Med History	Prosthesis related infection (Device related infection);
Unknown	Relevant Med History 2007	Middle cerebral artery infarct (Cerebral infarction);
Unknown	Relevant Med History Risk Factor- Aneurysm spurium after vascular partition	False aneurysm (Vascular pseudoaneurysm);
Unknown	Relevant Med History Risk Factor- Dec-2010	Prosthesis implantation (Prosthesis implantation);
Unknown	Relevant Med History	Smoker (Tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	ITALY	24	JAN	1921	91 Years	Female	55.00 kg	09	AUG	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Haemorrhagic ictus [Haemorrhagic stroke]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously, for the treatment of renal anaemia. This report describes a serious case of fatal
haemorrhagic ictus. This case from a physician (reference: It-038-0014) describes a 91-year-old female patient (weight: 55 kg and height: 150 cm) who received Retacrit (epoetin zeta, subcutaneous, 4000 UI once weekly; list and batch

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 11-AUG-2012
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 4000 IU, Freq: 1 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 16-DEC-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CARDICOR (BISOPROLOL FUMARATE) ; 22-JUN-2012 / Unknown
#2) COUMADIN /00014802/ (WARFARIN SODIUM) ; Unknown
#3) LASIX /00032601/ (FUROSEMIDE) ; 22-JUL-2011 / Unknown
#4) LUVION /00252501/ (CANRENOIC ACID) ; 22-JUL-2012 / Unknown
#5) PANTORC (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 26-SEP-2011 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1391691

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-AUG-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

number not reported) for renal anaemia from 16-Dec-2011 until 08-Aug-2012. Medical history included hypertension, atrial fibrillation, trauma (cut leg) on 24-Jul-2012 and significant and short weight changes due to fluid retention on 24-Jul-2012. The patient was not exposed to any other erythropoietin-stimulating agent (ESA). Concomitant medications included Cardicor (bisoprolol, 1.25 mg), Lasix (furosemide, 25 mg), Luvion (potassium canrenoate, 50 mg); all for heart failure, Coumadin (warfarin; dose not reported) for atrial fibrillation and Pantorc (pantoprazole, 40 mg) as prophylaxis, all given once a day. On 16-Dec-2011, the patient started treatment with epoetin zeta. The last dose given prior to the event was on 08-Aug-2012. On 09-Aug-2012, the patient experienced haemorrhagic ictus and was admitted to the hospital. Treatment for the adverse event was not reported. The patient died on 11-Aug-2012. Cause of death was haemorrhagic ictus. It was not reported if an autopsy was performed. The reporter's causality assessment between the event of haemorrhagic ictus and epoetin zeta was not related. English translation of the Italian diagnostic test result was received on 06-Sep-2012. Follow up report created to reflect additional information regarding diagnostic test. On an unknown date, cranial CT showed uneven acute subdural haematoma of the left hemisphere with maximum thickness of approximately 2.5 cm in the occipital-parietal lobes, and irregular signs of bleeding and signs of fluid-fluid level within context. Left falcotentorial haematoma. Thin layer of blood in left interhemispheric convexity. Signs of foaming with reduced view of left hemisphere cortical sulci and the perimesencephalic cistern, compression/dislocation of the third ventricle and the left lateral ventricle with rightward deviation of the median line by approximately 6 mm. Small traces of blood at left caudal thalamus. Left ventricular trigonal bleeding. Diffuse bilateral areas of chronic leukoencephalopathy. Calcifications of the carotid siphons. No signs of cranial fracture. Swelling of left side frontoparietal epicranial soft tissues with air bubbles. Hyperdensity of left ocular bulb, as with intrabulbar bleeding. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number. 23-Jan-2014: Data entry correction was made regarding laboratory data, concomitant medications, and suspect drug. Laboratory result of cranial CT was reflected in the laboratory section. In the narrative, active substance names of the concomitant medications should not be included as the information was not provided by the reporter. Frequencies of Cardicor, Lasix, Luvion, Coumadin, and Pantorc were reflected in the concomitant drugs section. The dose of epoetin zeta was corrected to 4000 UI and therapy end date was deleted in the suspect drug section. Action taken with epoetin zeta in response to the adverse event was not reported.

Case Comment: Overall case causality: Not related Given the patient's age and medical history, event is more likely due to natural pathophysiology of the disease. Overall case causality (Follow-up 18 Sep 2012): Not related No change in assessment

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Computerised tomogram head	Approximately 2.5 cm in occipitoparietal lobes,Unk	
2		Computerised tomogram head	As with intrabulbar bleeding,Unknown	
3		Computerised tomogram head	Chronic leukoencephalopathy,Unknown	
4		Computerised tomogram head	Cortical sulci and perimesencephalic cistern,Unkno	
5		Computerised tomogram head	Diffuse bilateral areas,Unknown	
6		Computerised tomogram head	In left interhemispheric convexity,Unknown	
7		Computerised tomogram head	Irregular signs of bleeding,Unknown	
8		Computerised tomogram head	Left hemisphere with maximum thickness,Unknown	
9		Computerised tomogram head	Left lateral ventricle with rightward deviation,Un	
10		Computerised tomogram head	No signs of cranial fracture,Unknown	
11		Computerised tomogram head	Of the median line by approximately 6mm,Unknown	

Mfr. Control Number: 1391691

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
12		Computerised tomogram head	Signs of fluid-fluid level within context,Unknown	
13		Computerised tomogram head	Small traces of blood at left caudal thalamus,Unkn	
14		Computerised tomogram head	Soft tissues with air bubbles,Unknown	
15		Computerised tomogram head	Uneven acute subdural haematoma,Unknown	
16		Computerised tomogram head	Thin layer of blood,Unknown	
17		Computerised tomogram head	Swelling of left side frontoparietal epicranial,Un	
18		Computerised tomogram head	Signs of foaming, reduced view of left hemisphere,	
19		Computerised tomogram head	Left ventricular trigonal bleeding,Unknown	
20		Computerised tomogram head	Left falcotentorial haematoma,Unknown	
21		Computerised tomogram head	Hyperdensity of left ocular bulb,Unknown	
22		Computerised tomogram head	Compression/dislocation of third ventricle,Unknown	
23		Computerised tomogram head	Calcifications of the carotid siphons,Unknown	

13. Relevant Tests

Cranial CT: Approximately 2.5 cm in occipitoparietal lobes, Unknown
Cranial CT: Left lateral ventricle with rightward deviation, Unknown
Cranial CT: Signs of foaming, reduced view of left hemisphere, Unknown
Cranial CT: Small traces of blood at left caudal thalamus, Unknown
Cranial CT: Swelling of left side frontoparietal epicranial, Unknown
Cranial CT: Cortical sulci and perimesencephalic cistern, Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. The patient was not exposed to any other eryhtropoietin-stimulating agent (ESA).
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor-24-Jul-2012	Fluid retention (Fluid retention);
Unknown	Relevant Med History Risk Factor-24-Jul-2012	Weight fluctuation (Weight fluctuation);
Unknown	Relevant Med History Risk Factor-24-Jul-2012	Leg traumatic amputation (Limb traumatic amputation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	30	APR	1936	76 Years	Male	Unk	20	DEC	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction. Epoetin zeta. Serious Hospira sponsored clinical study report from Sweden received from a physician (reference: Sw-018-0003) which refers to a 76-year-old Caucasian male patient (weight: 76 kg and height:
174 cm). Medical history included ischemic heart disease and hypertension. The patient was a former smoker/snuff user. He smoked 4-5 packets and stopped 50 years ago. Alcohol consumption was low and there was no known
hypersensitivities.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 20-DEC-2012
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 52 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 18-JUN-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CRESTOR (ROSUVASTATIN CALCIUM) Tablet ; Unknown
#2) ETALPHA (ALFACALCIDOL) Capsule ; Unknown
#3) FURIX (FUROSEMIDE) Tablet ; Unknown
#4) GLYTRIN (GLYCERYL TRINITRATE) ; Unknown
#5) IMDUR (ISOSORBIDE MONONITRATE) Tablet ; Unknown
#6) LOSARTAN (LOSARTAN) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1550791

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-NOV-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Additional medical history included cardiac infarction for several times, bypass operation also reported as CABG in 2000, PCI in five vessels in 2005, legionella in 2006 which was treated at ICU for 6 weeks; thereafter impaired renal function in 2008, dialysed for 1 year and was concluded in 2009, Iohexol clearance in Feb-2010 with GFR 18, type-2 diabetes, heart failure, severe vascular failure, chronic renal failure, and pancytopenia since spring of 2012.
The patient was referred to a rheumatologist in Sep-2012. The patient had been exposed to other erythropoetin-stimulating agent (ESA) Mircera (epoetin beta, 1315 ng/kg/week, once a month; route of administration not reported) for an unknown indication on 22-Nov-2010. Concomitant medications included sodium bicarbonate tablet (1 g, 1 x 1), Etalpha capsule (0.5 mcg, 1 x1), Trombyl tablet (75 mg, 1 x 1), Imdur delayed-release tablet (30 mg, 1 x 1), Furix tablet (40 mg, 1 x 1), bisoprolol tablet (5 mg, 1 x 1), Plendil tablet (5 mg, 1 x 1), Losartan tablet (50 mg, 1 x 1), Crestor tablet (20 mg, 1 x 1), Resonium oral/rectal suspension (dose not reported; 1 x 1), and Stilnoct tablet (5 mg, one at night as required) (routes of administration not reported for all); all given for unknown indications. The patient was enrolled in a Hospira-sponsored Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). On an 18-Jun-2012, the patient received epoetin zeta (52 IU/kg/week, once a week, subcutaenous; lot number not reported) for renal anaemia. Baseline laboratory data included B-Hb at 104 g/L (normal range: 134 to 170 g/L), B-EPC at 3.0 x 10^12/L (normal range: 4.2 to 5.7 x 10^12/L), B-LPC at 4.3 x 10^9/L (normal range: 3.5 to 8.8 x 10^9/L), B-TPC at 69 x 10^9/L (normal range: 145 to 350 x 10^9/L), Erc-MCH at 35 pg (normal range: 27 to 33 pg), Erc-MCV at 109 fl (normal range: 82 to 98 fl), and Erc-MCHC at 316 g/L (normal range: 330 to 360 g/L) on 08-Oct-2012 at 08:14. P-Potassium at 4.1 mmol/L (normal range: 3.2 to 4.6 mmol/L), P-creatinine at 223 mcmol/L (normal range: 60 to 105 mcmol/L), and P-Sodium at 141 mmol/L (normal range: 137 to 145 mmol/L) on 30-Oct-2012 at 08:23. B-Hb at 90 g/L, B-EPC at 2.5 x 10^12/L, B-LPC at 2.8 x 10^9/L, B-TPC at 49 x 10^9/L, Erc-MCH at 36 pg, Erc-MCV at 113 fl, Erc-MCHC at 323 g/L, B-neutrophil granulocytes at 1.3 x 10^9/L (normal range: 1.7 to 7.5 x 10^9/L), B-lymphocytes at 1.2 x 10^9/L (normal range: 1.1 to 4.8 x 10^9/L), B-monocytes at 0.2 x 10^9/L (normal range: 0.1 to 1.0 x 10^9/L), B-eosinophil granulocytes at 0.02 x 10^9/L (normal range: 0.0 to 0.6 x 10^9/L), B-basophil granulocytes at 0.00 x 10^9/L (normal range: 0.0 to 0.2 x 10^9/L), P-albumin at 44 g/L (normal range: 34 to 45 g/L), P-calcium at 2.28 mmol/L (normal range: 2.10 to 2.55 mmol/L), P-Ca corrected at 2.22 mmol/L (normal range: 2.10 to 2.55 mmol/L), P-CRP at 5.9 mg/L (normal value: less than 4.0 mg/L), P-phosphate at 1.45 mmol/L (normal range: 0.75 to 1.40 mmol/L), P-HDLcholesterol at 0.7 mmol/L (normal value: greater than 1.0 mmol/L), P-potassium at 5.1 mmol/l, P-cholesterol at 2.1 mmol/L (normal value: less than 5 mmol/L), P-creatinine at 277 mcmol/L, P-LDL-cholesterol at less than 1.5 mmol/L (normal value: less than 3.0 mmol/l), P-sodium at 141 mmol/L, fP-triglycerides at 1.9 mmol/L (normal value less than 2 mmol/L), P-Urea at 23.3 mmol/L (normal range: 3.5 to 8.2 mmol/L), U-Creatinine N at 4.9 mmol/L (normal range not reported), UAlb/Crea index at 108.2 g/mol (normal value less than 5.0 g/mol), U-Glucose test strip negative (normal value less than 5.5 mmol/L), U-ketones test strip negative (normal value less than 1.5 mmol/L), U-Ery/Hb test strip negative (normal value less than 25 ery/mcL, U-pH strip 7.0 (unit of measurement not reoported; normal range: 5 - 6), U-protein strip with Ca 1.0 g/L (normal value less than 0.3 g/L), U-nitrite negative (normal value negative), U-leucocytes test strip negative (normal value less than 15 leuk/mcL), and B-HbA1c-DCA at 50 mmol/mc (normal range: 31 to 46 mmol/mc) on 22-Nov-2012 at 08:59. B-hb at 88 g/L, B-LPC at 2.6 x 10^9/L, B-TPC at 39 x 10^9/L, P-albumin at 45 g/L, P-calcium at 2.29 mmol/L, P-Ca corrected at 2.20 mmol, P-CRP at 6.1 mg/L, P-potassium at 4.9 mmol/L, P-creatinine at 262 mcmol/L, P-sodium at 142 mmol/L, P-APT time at 36 s (normal range: 29 to 42 s), P-PK at 1.2 INR (normal range: 0.9 to 1.1 INR), P-tropenin-I at 0.057 mcg/L (normal value less than 0.070 mcg/L), vB-pH at 7.33 (normal range: 7.26 to 7.40), vB-pCO2 at 5.1 kPa (normal range: 5.5 to 9.0 kPa), vB-base excess at -5 mmol/L (normal range: -2 to +3 mmol/L), vP-glucose at 9.2 mmol/L (normal range: 4.0 to 7.5 mmol/L), and vA-bicarbonate status at 19 mmol/L (normal range: 22 to 26 mmol/L) on the same day of 22-Nov-2012 at 09:43. P-tropenin-I was at 0.048 mcg/L on 22-Nov-2013 at 15:00. B-Hb at 101 g/L, B-EPC at 2.9 x 10^12/L, B-LPC at 2.4 x 10^9/L, P-TPC at 36 x 10^9/L, Erc-MCH at 34 pg, Erc-MCV at 105 fl, Erc-MCHC at 327 g/L, P-CRP at 8.3 mg/L, P-potassium at 4.8 mmol/L, P-creatinine at 239 mcmol/L, P-sodium at 140 mmol/L, and P-urea at 21.8 mmol/L on 23-Nov-2012 at 07:30. B-TPC at 47 x 10^9/L on 27-Nov-2012 at 08:29. B-Hb at 106 g/L, B-LPC at 2.9 x 10^9/L, B-TPC at 38 x 10^9/L, P-albumin at 45 g/L, P-calcium at 2.25 mmol/L, P-calcium corrected at 2.18 mmol/L, P-CRP at less than 25 ery/mcL, U-pH strip 7.0 (unit of measurement not reoported; normal range: 5 - 6), U-protein strip with Ca 1.0 g/L (normal value less than 0.3 g/L), U-nitrite negative (normal value negative), U-leucocytes test strip negative (normal value less than 15 leuk/mcL), and B-HbA1c-DCA at 50 mmol/mc (normal range: 31 to 46 mmol/mc) on 22-Nov-2012 at 08:59. B-hb at 88 g/L, B-LPC at 2.6 x 10^9/L, B-TPC at 39 x 10^9/L, P-albumin at 45 g/L, P-calcium at 2.29 mmol/L, P-Ca corrected at 2.20 mmol, P-CRP at 6.1 mg/L, P-potassium at 4.9 mmol/L, P-creatinine at 262 mcmol/L, P-sodium at 142 mmol/L, P-APT time at 36 s (normal range: 29 to 42 s), P-PK at 1.2 INR (normal range: 0.9 to 1.1 INR), P-tropenin-I at 0.057 mcg/L (normal value less than 0.070 mcg/L), vB-pH at 7.33 (normal range: 7.26 to 7.40), vB-pCO2 at 5.1 kPa (normal range: 5.5 to 9.0 kPa), vB-base excess at -5 mmol/L (normal range: -2 to +3 mmol/L), vP-glucose at 9.2 mmol/L (normal range: 4.0 to 7.5 mmol/L), and vA-bicarbonate status at 19 mmol/L (normal range: 22 to 26 mmol/L) on the same day of 22-Nov-2012 at 09:43. P-tropenin-I was at 0.048 mcg/L on 22-Nov-2013 at 15:00. B-Hb at 101 g/L, B-EPC at 2.9 x 10^12/L, B-LPC at 2.4 x 10^9/L, P-TPC at 36 x 10^9/L, Erc-MCH at 34 pg, Erc-MCV at 105 fl, Erc-MCHC at 327 g/L, P-CRP at 8.3 mg/L, P-potassium at 4.8 mmol/L, P-creatinine at 239 mcmol/L, P-sodium at 140 mmol/L, and P-urea at 21.8 mmol/L on 23-Nov-2012 at 07:30. B-TPC at 47 x 10^9/L on 27-Nov-2012 at 08:29. B-Hb at 106 g/L, B-LPC at 2.9 x 10^9/L, B-TPC at 38 x 10^9/L, P-albumin at 45 g/L, P-calcium at 2.25 mmol/L, P-calcium corrected at 2.18 mmol/L, P-CRP at 1.2 mg/L, p-phosphate at 1.18 mmol/L, P-potassium at 3.9 mmol/L, P-creatinine at 230 mcmol/L, P-sodium at 140 mmol/L, and P-urea at 21.8 mmol/L on 05-Dec-2012 at 10:18. On 17-Dec-2012, the patient was admitted with impaired and poor general health with no cause. The patient had increasing dyspnoea and tightness in the chest which the patient has had for around 2 days. Tightness in the chest responded to Glytrin sublingual spray 0.4 mg/dose (1-2 doses as required)

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

but the problem had not completely resolved. The patient experienced vomiting 4 days ago. The patient was not feeling sick but has had cough with some mucous production. The patient also had renal failure and multiple vascular failure. The patient also had anemia. The patient was given blood due to low hemoglobin. Laboratory examination on 17-Dec-2012 at 10:36 included TNI negative, B-Hb was 77 g/L, B-LPC was 2.0 x 10^9/L, B-TPC was 36 x 10^9/L, P-PK was 1.5 INR, pCO2 was 4.9 kPa, vA-bicarbonate status was 19 mmol/L, vP-glucose was 11.0 mmol/L, vB-lactate was 2.6 also reported as 2.5 mmol/L (normal range: 0.7 to 2.1 mmol/L), P-ASAT was 0.83 mckat/L (normal range: 0.20 to 0.60 mckat/L), PCRP was 16 also reported as 18 mg/L, P-potassium was 4.8 also reported as 4.6 mmol/L, P-creatinine was 242 mcmol/L, P-ALAT at 0.58 mckat/L (normal value less than 1.1 mckat/L), P-albumin at 40 g/L, p-ALP at 0.9 mckat/L (normal range: 0.6 to 1.8 mckat/L), P-bilirubin at 23 mcmol/L (normal value less than 25 mcmol/L), P-calcium at 2.16 mmol/L, P-calcium corrected at 2.18 mmol/L, P-sodium at 140 mmol/L, P-lipase at 2.0 mckat/L (normal range: 0.4 to 5.0 mckat/L), P-APT at 30 s, vB-pH at 7.34, and vB-base excess at -5. General state of health of the patient on the same day of 17-Dec-2012, at 10.55 was reported as pale, slightly dyspnoeic at rest, respiratory saturation of 92%, respiratory rate of 22, saturation at 1L oxygen was 96%, afebrile, with occasional signs of bleeding, slight bruising on the left lower arm, heart was arrhythmic, heart rate was 80/min, no audible murmurs, lungs with vesicular breathing sounds, no rattling (illegible), abdomen as soft and non-tender, and leg had no oedema. ECG of the patient showed atrial fibrillation, heart rate at 82 (unit not reported), left-sided branch block, negative T in aVL, aVR, diversion (illegible) and V4-V6 (none of these were new events). At 11:13 of the same day, P-tropenin-I was 0.045 mcg/L, 0.044 mcg/L at 14:54, and 0.048 mcg/L at 20:00. It was reported that initially, the patient was admitted to department 5 for blood transfusion. It was reported that Hb was around 100 after blood transfusion. However, due to chest pains and ECG, TNI series also followed and the patient was admitted for telemetry. There was also increasing TNI in connection with onset of chest pains. Oxygen treatment was given as required and target saturation was 94% or more. The patient also had (illegible) and thrombocytopenia which were seen previously but never when the results were so low. ASAT was slightly over the limit and high for the first time. PC of 1.6 (unit of measurement not reported) was spontaneous and not related to warfarin treatment as the patient was not taking any warfarin. It was also reported that warfarin was discontinued due to thrombocytopenia. On 18-Dec-2012, at 07:30, B-Hb was 120 g/L. On 19-Dec-2012, at 07:30, B-Hb was 91 g/L and B-TPC was 29 x 10^9/L; while B-Hb was 98 g/L at 23:58 of the same day. On the evening of 20-Dec-2012, the patient had myocardial infarction. During the evening/night at 00.34, the patient was panting and appeared breathless but was still responsive and oriented. The patient had respiratory frequency of around 30 (unit of measurement not reported) but retained good respiratory saturation. It was also reported that the patient experienced ongoing fatigue and tiredness. The patient experienced fibrillation which he also had at the time of admittance but which was now tachycardic with pulse at 120-140 (unit of measurement not reported). The patient complained of chest pain but was pain-free on Glytrin. The patient also had tightness in the chest which he already had upon admittance so this was not therefore a new event. Troponin series was negative. There was tachypnoea and vesicular breathing sounds bilaterally. Acute Hb was 98 (unit of measurement not reported) which was acceptable considering the figure was 91 earlier in the day. The patient rapidly developed atrial fibrillation but maintained blood pressure. There was accelerated Hb and well saturated. The patient received extra bisoprolol (5 mg, route of administration not reported) to reduce pulse. No further actions in present condition and the on-call doctor was informed. On the same day of 20-Dec-2012, at 03.22, patient sufferred from continuous pains which were poorly managed with Glytrin. As the patient's heart rate dropped spontaneously, he had only received half of bisopolol extra (i.e. 2.5 mg). Saturation was still good but heart rate later rose again to around 140-160 (unit of measurement not reported). Blood pressure dropped to around 100 and the patient underwent telemetry. The patient's pains became more frequent and the patient was administered morphine injection (dose not reported). When the patient had awaken, the pulse rose to 170 (unit of measurement not reported) and systolic blood pressure later dropped to 80 (unit of measurement not reported). On 20-Dec-2012, at 03:54, BHb, VA was 97 g/L (normal range: 137 to 170 g/L), aB-Ca, free VA was 1.13 mmol/L (normal range: 1.20 to 1.35 mmol/L), aP-Glucose, VA was 4.4 mmol/L (normal range: 4.0 to 7.5 mmol/L), aB-Potassium, VA was 5.9 mmol/L (normal range: 3.2 to 4.6 mmol/L), aB-chlorides, Va was 109 mmol/L (normal range: 100 to 110 mmol/L), aB-lactate, VA was 11.2 mmol/L (normal range: 0.5 to 1.6 mmol/L), aB-sodium, VA was 134 mmol/L (normal range: 137 to 145 mmol/l), aB-pH, VA was 7.14 (unit not reported; normal range: 7.36 to 7.44), aB-pCO2, VA was 3.1 kPa (normal range: 4.7 to 5.9 kPa), aB-pO2, VA was 10.8 kPa (normal range: 8.0 to 9.2 kPa), aB-base excess, stat. VA was -19.9 mmol/L (normal range: -1.5 to +3 mmol/L), VA was 90% (normal range: 92 to 99%), aB-bicarb. curr, VA was 8 mmol/L (normal range: 21 to 28 mmol/L, aB-COHb, VA was less than 1.0% (normal value less than 1.0%), aB-MetHb, VA was 1.6% (normal value less than 2.0%), aB-FO2(1), VA was 80.0% (normal value not reported), and aB-pO2/FO2-quot, VA was 13.5 kPa (normal value not reported). On the same day, at 03:55, B-Hb was 95 g/L, B-LPC was 3.9 x 10^9/L, B-TPC was 27 x 10^9/L, P-ALAT was 16.5 mckat/L, P-albumin was 36 g/L, P-ALP was 1.0, P-bilirubin was 22 mcmol/L, P-calcium was 2.02 mmol/L, P-calcium corrected was 2.12 mmol/L, P-CRP was 56 mg/L, P-potassium was 6.0 mmol/L, P-creatinine was 335 mcmol/L, P-LD was 37 mckat/L, p-lipase was 3.0 mckat/L, P-sodium was 136 mmol/L, P-urea was 28.0 mmol/L, and P-tropenin-I was 0.193 mcg/L. Still on the same day, at 03:56, P-APT time was 48 s, P-D-dimer was 17.8 mg/L (normal value less than 0.5 mg/L), and P-PC was 2.3 INR. The patient started to make progress in the ICU and the on-call doctor and anaesthetist were informed. The on-call cardiologist was also consulted. The patient's condition was not considered to be suitable for PCI treatment in case of (illegible). It was thought that the priority that night was to control the patient's heart rate below 100. The patient was given cordarone (150 mg, route of administration not reported) which was administered with caution. It was reported that the patient also received inotropic drugs and intravenous fluids (doses and routes of administration not reported). It may be well that the patient's blood pressure fell but this was a risk that must be taken. The patient was moved to the ICU after ICU patients were relocated. It was reported that the patient's thrombocytes were around 30 and potassium also increased during the entire period of care from 17-Dec-2012 until 20-Dec-2012. It was reported that the patient's condition deteriorated steadily during autumn and there was no troponin concentration suggesting cardiac ischaemia. On 20-Dec-2012, at 11.10, the patient experienced fluctuating chest pains and after several hours, circulatory insufficiency with falling blood pressure and asystole. May have been aortic dissection or pulmonary embolism. It was also reported

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

that the patient experienced severe vascular failure resulting in death due to circulatory failure after episodes of chest pains. The patient died on 20-Dec-2012. Cause of death was myocardial infarction. The patient wished no autopsy should be performed. The reporter's opinion of causality for the event of fatal myocardial infarction in relation to epoetin zeta was not assessable. Risk factor inlcuded coronary heart disease and diabetes type 2. The following information was unable to provide by the reporter for indentification and traceability of the biosimilar product Retacrit: batch number. 24-May-2013: Follow up report was received from the investigator. The adverse event was updated to fatal myocardial infarction (previously reported as fatal heart disease). Proprietary Medicinal Product name of epoetin zeta was selected. Structured dosage form and action taken fields were populated for epoetin zeta. This information has been incorporated in the narrative and in the corresponding data fields. 13-Nov-2013: Additional information was received from the same reporter. Follow up report was created to reflect new information that patient was a 76-year-old Caucasian male; heart disease and hypertension were added as a medical history; the patient had been exposed to other erythropoetinstimulating agent (ESA) Mircera (once a month; dose and route of administration not reported) until Jun-2012 for an unknown indication; frequency and therapy date of epoetin zeta was added; onset date of adverse event was added; and reporter's causality assessment; reporter's causality assessment of the event of fatal myocardial infarction in relation to epoetin zeta was not assessable. This information has been incorporated in the narrative and in the corresponding data fields. 05-Dec-2013: Additional information was received from the same reporter. Follow up report was created to reflect new information that the patient was a smoker, with low alcohol consumption and with no known allergies. Cardiac infarction, bypass operation, PCI in five vessels, legionella, impaired renal function, dialysis, type-2 diabetes, heart failure, severe vascular failure, chronic renal failure, and pancytopenia were added as medical history. Sodium bicarbonate, Etalpha, Trombyl, Imdur, Furix, bisoprolol, Plendil, Losartan, Crestor, Resonium, and Stilnoct were added as concomitant medications. Baseline laboratory and diagnostic tests were added. Detailed information regading adverse event was also added. This information has been incorporated in the narrative and in the corresponding data fields. 26-Nov-2014: Additional information was received from the same reporter. Follow-up report was created to reflect new information regarding patient's weight and height; coronary heart disease was added as a risk factor; dose of Mircera and epoetin zeta were also added. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without further objective clinical event details, circumstances surrounding patient death, medical history and concomitant medications. - N. Gonzales (07 Jan 2013) Follow-up (28 May 2013): New reported adverse event noted, but still not enough details available to provide a causality assessment. - N. Gonzales Follow-up: No change in previous causality assessment. - N. Gonzales (18 Nov 2013) Follow-up: New information noted. Causality upgraded to possible. Although patient has multiple cardiovascular risk factors in the medical history, suspect drug can still theoretically increase the incidence of thrombosis and infarction by increasing red blood cell concentration. Cannot rule out its possible contributory effect. - N. Gonzales (19 Dec 2013) Follow-up: New information noted, but does not warrant change in previous causality assessment. - N. Gonzales (04 Dec 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	22-NOV-2012	Activated partial thromboplastin time	36 s, Unknown	42 29
2	17-DEC-2012	Activated partial thromboplastin time	30 s, Unknown	42 29
3	20-DEC-2012	Activated partial thromboplastin time	48 s, Unknown	42 29
4	17-DEC-2012	Alanine aminotransferase	0.58 mckat/L, Unknown	
5	20-DEC-2012	Alanine aminotransferase	16.5 mckat/L,Unknown	
6	17-DEC-2012	Aspartate aminotransferase	0.83 mckat/L, Unknown	2.55 0.20
7	22-NOV-2012	Base excess	-5 mmol	+3 -2
8	17-DEC-2012	Base excess	-5 mmol	+3 -2
9	20-DEC-2012	Base excess	-19.9 mmol/l	3 -1.5
10	22-NOV-2012	Basophil count	0.00 x10 9/l	0.2 0.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
11	22-NOV-2012	Blood albumin	44 g/l	45 34
12	22-NOV-2012	Blood albumin	45 g/l	45 34
13	05-DEC-2012	Blood albumin	45 g/l	45 34
14	17-DEC-2012	Blood albumin	40 g/l	45 34
15	20-DEC-2012	Blood albumin	36 g/l	45 34
16	17-DEC-2012	Blood alkaline phosphatase	0.9 mckat/L, Unknown	1.8 0.6
17	20-DEC-2012	Blood alkaline phosphatase	1.0 mckat/L, Unknown	1.8 0.6
18	22-NOV-2012	Blood bicarbonate	19 mmol/l	26 22
19	17-DEC-2012	Blood bicarbonate	19 mmol/l	26 22
20	20-DEC-2012	Blood bicarbonate	8 mmol/l	28 21
21	17-DEC-2012	Blood bilirubin	23, MCMOL/L	
22	20-DEC-2012	Blood bilirubin	22, MCMOL/L	
23	22-NOV-2012	Blood calcium	2.29 mmol/l	2.55 2.10
24	22-NOV-2012	Blood calcium	2.22 mmol/l	2.55 2.10
25	22-NOV-2012	Blood calcium	2.20 mmol/l	2.55 2.10
26	22-NOV-2012	Blood calcium	2.28 mmol/l	2.55 2.10
27	05-DEC-2012	Blood calcium	2.18 mmol/l	2.55 2.10
28	05-DEC-2012	Blood calcium	2.25 mmol/l	2.55 2.10
29	17-DEC-2012	Blood calcium	2.18 mmol/l	2.55 2.10
30	17-DEC-2012	Blood calcium	2.16 mmol/l	2.55 2.10
31	20-DEC-2012	Blood calcium	2.02 mmol/l	2.55 2.10
32	20-DEC-2012	Blood calcium	2.12 mmol/l	2.55 2.10
33	20-DEC-2012	Blood chloride	109 mmol/l	110 100
34	22-NOV-2012	Blood cholesterol	2.1 mmol/l	
35	30-OCT-2012	Blood creatinine	262, MCMOL/L	105 60
36	30-OCT-2012	Blood creatinine	223, MCMOL/L	105 60

Mfr. Control Number: 1550791

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
37	22-NOV-2012	Blood creatinine	277, MCMOL/L	105 60
38	23-NOV-2012	Blood creatinine	239, MCMOL/L	105 60
39	05-DEC-2012	Blood creatinine	230, MCMOL/L	105 60
40	17-DEC-2012	Blood creatinine	242, MCMOL/L	105 60
41	20-DEC-2012	Blood creatinine	335, MCMOL/L	105 60
42	22-NOV-2012	Blood glucose	9.2 mmol/l	7.5 4.0
43	17-DEC-2012	Blood glucose	11.0 mmol/l	7.5 4.0
44	20-DEC-2012	Blood glucose	4.4 mmol/l	7.5 4.0
45	17-DEC-2012	Blood lactic acid	2.5 mmol/l	2.1 0.7
46	17-DEC-2012	Blood lactic acid	2.6 mmol/l	2.1 0.7
47	20-DEC-2012	Blood lactic acid	11.2 mmol/l	1.6 0.5
48	20-DEC-2012	Blood methaemoglobin	1.6 %	
49	22-NOV-2012	Blood pH	7.33, Unknown	7.40 7.26
50	17-DEC-2012	Blood pH	7.34, Unknown	7.40 7.26
51	22-NOV-2012	Blood phosphorus	1.45 mmol/l	1.40 0.75
52	05-DEC-2012	Blood phosphorus	1.18 mmol/l	1.40 0.75
53	30-OCT-2012	Blood potassium	4.1 mmol/l	4.6 3.2
54	30-OCT-2012	Blood potassium	4.9 mmol/l	4.6 3.2
55	22-NOV-2012	Blood potassium	5.1 mmol/l	4.6 3.2
56	23-NOV-2012	Blood potassium	4.8 mmol/l	4.6 3.2
57	05-DEC-2012	Blood potassium	3.9 mmol/l	4.6 3.2
58	17-DEC-2012	Blood potassium	4.6 mmol/l	4.6 3.2
59	17-DEC-2012	Blood potassium	4.8 mmol/l	4.6 3.2
60	20-DEC-2012	Blood potassium	6.0 mmol/l	4.6 3.2
61	20-DEC-2012	Blood potassium	5.9 mmol/l	4.6 3.2
62	20-DEC-2012	Blood pressure measurement	Dropped to 100, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
63	20-DEC-2012	Blood pressure systolic	Dropped to 80, Unknown	
64	30-OCT-2012	Blood sodium	142 mmol/l	145 137
65	30-OCT-2012	Blood sodium	141 mmol/l	145 137
66	22-NOV-2012	Blood sodium	141 mmol/l	145 137
67	23-NOV-2012	Blood sodium	140 mmol/l	145 137
68	05-DEC-2012	Blood sodium	140 mmol/l	145 137
69	17-DEC-2012	Blood sodium	140 mmol/l	145 137
70	20-DEC-2012	Blood sodium	134 mmol/l	145 137
71	20-DEC-2012	Blood sodium	136 mmol/l	145 137
72	22-NOV-2012	Blood triglycerides	1.9 mmol/l	
73	22-NOV-2012	Blood urea	23.3 mmol/l	8.2 3.5
74	23-NOV-2012	Blood urea	21.8 mmol/l	8.2 3.5
75	05-DEC-2012	Blood urea	21.8 mmol/l	8.2 3.5
76	20-DEC-2012	Blood urea	28.0 mmol/l	8.2 3.5
77	17-DEC-2012	Breath sounds	Vesicular breathing sounds, no rattling, Unknown	
78	20-DEC-2012	Breath sounds	Vesicular breathing sounds bilaterally, Unknown	
79	22-NOV-2012	C-reactive protein	5.9 mg/l	
80	22-NOV-2012	C-reactive protein	6.1 mg/l	
81	23-NOV-2012	C-reactive protein	8.3 mg/l	
82	05-DEC-2012	C-reactive protein	1.2 mg/l	
83	17-DEC-2012	C-reactive protein	18 mg/l	
84	17-DEC-2012	C-reactive protein	16 mg/l	
85	20-DEC-2012	C-reactive protein	56 mg/l	
86	20-DEC-2012	Carboxyhaemoglobin	less than 1.0 %	
87		Coagulation test	1.6, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
88	22-NOV-2012	Coagulation test	1.2 INR, Unknown	1.1 0.9
89	17-DEC-2012	Coagulation test	1.5 INR, Unknown	1.1 0.9
90	20-DEC-2012	Coagulation test	2.3 INR, Unknown	1.1 0.9
91	22-NOV-2012	Creatinine urine	4.9 mmol/l	
92	17-DEC-2012	Electrocardiogram	Negative T in aVL,aVR,v4-v6, Unknown	
93	22-NOV-2012	Eosinophil count	0.02 x10 9/l	0.6 0.0
94	20-DEC-2012	Fibrin D dimer	17.8 mg/l	
95	17-DEC-2012	General physical condition	leg had no oedema, Unknown	
96	17-DEC-2012	General physical condition	Pale, slightly dyspnoeic at rest, afebrile,Unknown	
97	17-DEC-2012	General physical condition	with occasional signs of bleeding, Unknown	
98	17-DEC-2012	General physical condition	slight bruising on the left lower arm, Unknown	
99	22-NOV-2012	Glucose urine	Negative, Unknown	
100	22-NOV-2012	Glycosylated haemoglobin	50 mmol/mc, Unknown	46 31
101	08-OCT-2012	Haemoglobin	104 g/l	170 134
102	22-NOV-2012	Haemoglobin	88 g/l	170 134
103	22-NOV-2012	Haemoglobin	90 g/l	170 134
104	23-NOV-2012	Haemoglobin	101 g/l	170 134
105	05-DEC-2012	Haemoglobin	106 g/l	170 134
106	17-DEC-2012	Haemoglobin	77 g/l	170 134
107	18-DEC-2012	Haemoglobin	120 g/l	170 134
108	19-DEC-2012	Haemoglobin	98 g/l	170 134
109	19-DEC-2012	Haemoglobin	91 g/l	170 134
110	20-DEC-2012	Haemoglobin	97 g/l	170 137
111	20-DEC-2012	Haemoglobin	98, Unknown	
112	20-DEC-2012	Haemoglobin	95 g/l	170 134
113	20-DEC-2012	Haemoglobin	91, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
114	22-NOV-2012	Haemoglobin urine	Negative, Unknown	
115	17-DEC-2012	Heart rate	80/min; arrhythmic, Unknown	
116	17-DEC-2012	Heart rate	82, Unknown	
117	20-DEC-2012	Heart rate	140-160, Unknown	
118	20-DEC-2012	Heart rate	170, Unknown	
119	20-DEC-2012	Heart rate	120-140, Unknown	
120	17-DEC-2012	Heart sounds	No audible murmurs, Unknown	
121	22-NOV-2012	High density lipoprotein	0.7 mmol/l	
122	20-DEC-2012	Laboratory test	13.5, KPA	
123	20-DEC-2012	Laboratory test	90 %	99 92
124	20-DEC-2012	Laboratory test	80.0 %	
125	20-DEC-2012	Laboratory test	37 mckat/L, Unknown	
126	20-DEC-2012	Laboratory test	1.13 mmol/l	1.35 1.20
127	17-DEC-2012	Lipase	20 mckat/L, MCG/L	5.0 0.4
128	20-DEC-2012	Lipase	3.0 mckat/L, Unknown	5.0 0.4
129	22-NOV-2012	Low density lipoprotein	less than 1.5 mmol/l	
130	22-NOV-2012	Lymphocyte count	1.2 x10 9/l	4.8 1.1
131	08-OCT-2012	Mean cell haemoglobin	35 pg	33 27
132	22-NOV-2012	Mean cell haemoglobin	36 pg	33 27
133	23-NOV-2012	Mean cell haemoglobin	34 pg	33 27
134	08-OCT-2012	Mean cell haemoglobin concentration	316 g/l	360 330
135	22-NOV-2012	Mean cell haemoglobin concentration	323 g/l	360 330
136	23-NOV-2012	Mean cell haemoglobin concentration	327 g/l	360 330
137	08-OCT-2012	Mean cell volume	109, FL	98 82
138	22-NOV-2012	Mean cell volume	113, FL	98 82

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
139	23-NOV-2012	Mean cell volume	105, FL	98 82
140	22-NOV-2012	Monocyte count	0.2 x10 9/l	1.0 0.1
141	22-NOV-2012	Neutrophil count	1.3 x10 9/l	7.5 1.7
142	22-NOV-2012	Nitrite urine	Nrgative, Unknown	
143	17-DEC-2012	Oxygen saturation	92 %	
144	17-DEC-2012	Oxygen saturation	96 %	
145	20-DEC-2012	Oxygen saturation	Good, Unknown	
146	22-NOV-2012	PCO2	5.1, KPA	9.0 5.5
147	17-DEC-2012	PCO2	4.9,KPA	9.0 5.5
148	20-DEC-2012	PCO2	3.1, KPA	5.9 4.7
149	20-DEC-2012	PO2	10.8, KPA	9.2 8.0
150	17-DEC-2012	Physical examination	Soft and non-tender, Unknown	
151	08-OCT-2012	Platelet count	69 x10 9/l	350 145
152	22-NOV-2012	Platelet count	49 x10 9/l	350 145
153	22-NOV-2012	Platelet count	39 x10 9/l	350 145
154	23-NOV-2012	Platelet count	36 x10 9/l	350 145
155	27-NOV-2012	Platelet count	47 x10 9/l	350 145
156	05-DEC-2012	Platelet count	38 x10 9/l	350 145
157	17-DEC-2012	Platelet count	36 x10 9/l	350 145
158	19-DEC-2012	Platelet count	29 x10 9/l	350 145
159	20-DEC-2012	Platelet count	27 x10 9/l	350 145
160	22-NOV-2012	Protein urine	with Ca 1.0 g/l	
161	08-OCT-2012	Red blood cell count	3.0 x10 12/l	5.7 4.2
162	22-NOV-2012	Red blood cell count	2.5 x10 12/l	5.7 4.2
163	23-NOV-2012	Red blood cell count	2.9 x10 12/l	5.7 4.2
164	17-DEC-2012	Respiratory rate	22, Unknown	

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ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
165	20-DEC-2012	Respiratory rate	30, Unknown	
166	20-DEC-2012	Troponin	Negative, Unknown	
167	22-NOV-2012	Troponin I	0.048, MCG/L	
168	22-NOV-2012	Troponin I	0.057, MCG/L	
169	17-DEC-2012	Troponin I	0.048, MCG/L	
170	17-DEC-2012	Troponin I	0.044, MCG/L	
171	17-DEC-2012	Troponin I	Negative, Unknown	
172	17-DEC-2012	Troponin I	0.045, MCG/L	
173	20-DEC-2012	Troponin I	0.193, MCG/L	
174	22-NOV-2012	Urine albumin/creatinine ratio	108.2 g/mol, Unknown	
175	22-NOV-2012	Urine ketone body	Negative, Unknown	
176	08-OCT-2012	White blood cell count	4.3 x10 9/l	8.8 3.5
177	22-NOV-2012	White blood cell count	2.8 x10 9/l	8.8 3.5
178	22-NOV-2012	White blood cell count	2.6 x10 9/l	8.8 3.5
179	23-NOV-2012	White blood cell count	2.4 x10 9/l	8.8 3.5
180	05-DEC-2012	White blood cell count	2.9 x10 9/l	8.8 3.5
181	17-DEC-2012	White blood cell count	2.0 x10 9/l	8.8 3.5
182	20-DEC-2012	White blood cell count	3.9 x10 9/l	8.8 3.5
183	22-NOV-2012	White blood cells urine	Negative, Unknown	
184	22-NOV-2012	pH body fluid	7.0, Unknown	6 5
185	20-DEC-2012	pH body fluid	7.14, Unknown	7.44 7.36

13. Relevant Tests

ECG(17-Dec-2012):Atrial fibrillation, left-sided branch block Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution	52 IU/kg, Freq: 1 Week;	Renal anaemia (Nephrogenic	18-JUN-2012 /

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
for injection {Lot # UNK}; Regimen #1	Interval: 1; Subcutaneous	anaemia)	Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) PLENDIL (FELODIPINE) Tablet ; Unknown

#8) RESONIUM (SODIUM POLYSTYRENE SULFONATE) ; Unknown

#9) STILNOCT (ZOLPIDEM TARTRATE) Tablet ; Unknown

#10) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; Unknown

#11) BISOPROLOL (BISOPROLOL) Tablet ; Unknown

#12) SODIUM BICARBONATE (SODIUM BICARBONATE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient was a former smoker/snuff user. He smoked 4-5 packets and stopped 50 years ago. Alcohol consumption was low and there was no known hypersensitivities. Additional medical history included cardiac infarction for several times, bypass operation also reported as CABG in 2000, PCI in five vessels in 2005, legionella in 2006 which was treated at ICU for 6 weeks; thereafter impaired renal function in 2008, dialysed for 1 year and was concluded in 2009, Iohexol clearance in Feb-2010 with GFR 18, type-2 diabetes, heart failure, severe vascular failure, chronic renal failure, and pancytopenia since spring of 2012. The patient was referred to a rheumatologist in Sep-2012. Medical history also included ischemic heart disease and hypertension. The patient had been exposed to other erythropoetin-stimulating agent (ESA) Mircera (1315 ng/kg/week, once a month; route of administration not reported) until Jun-2012 for an unknown indication. The patient did not experience any thromboembolic event during treatment with other ESA. Risk factor included coronary heart disease. The patient died on 20-Dec-2012. Cause of death was myocardial infarction. The patient wished no autopsy should be performed. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History 2008	Impaired renal function (Renal impairment);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Pancytopenia (Pancytopenia);
Unknown to Ongoing	Relevant Med History	Vascular disorder (Angiopathy);
Unknown	Relevant Med History	Alcohol use (Alcohol use);
Unknown	Relevant Med History	CABG (Coronary artery bypass);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);

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ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History Concluded in 2009	Dialysis (Dialysis);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Ex-tobacco user (Ex-tobacco user);
Unknown	Relevant Med History 2006	Legionella infection (Legionella infection);
Unknown	Relevant Med History 2005	Percutaneous coronary intervention (Percutaneous coronary intervention);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
22-NOV-2010 to Unknown	Past Drug Event	MIRCERA (MIRCERA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	FRANCE	06	SEP	1920	92 Years	Female	86.50 kg	08	APR	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Stroke accident [Cerebrovascular accident]

Case Description: This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal hemorrhagic accident of
anticoagulant medication and fatal stroke. This serious case from an investigator (ref: Fr-064-0019) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency, formulation, and

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 10-APR-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 Freq: 1 Week: Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 26-OCT-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) HEPARIN (HEPARIN) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History ongoing	Breast cancer (Breast cancer)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1685920

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-MAY-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

batch number not reported) for renal anemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced hemorrhagic accident of anticoagulant medication and stroke. Action taken with suspect drug and treatment for the adverse events was not reported. The patient died on 10-Apr-2013. Causes of death were hemorrhagic accident of anticoagulant medication and stroke. It was not reported if an autopsy was performed. The reporter's causality assessment for the events of fatal hemorrhagic accident of anticoagulant medication and fatal stroke in relation to epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number, date of expiry, and previous exposure to other biosimilars. 21-May-2013: Follow-up information received from the investigator. Follow-up report created to reflect additional information regarding patient details, medical history, concomitant medication, suspect drug, laboratory tests, adverse events and reporter's causality assessment. Adverse event was changed to fatal stroke accident (previously reported as fatal hemorrhagic accident of anticoagulant medication and fatal stroke). Patient was a 92-year-old female patient (weight: 86.5 kg and height: 152 cm). Patient's date of birth and ethnic origin were reported. The patient was obese with BMI of 37.4 kg/m^2. The patient has no history of smoking. Other risk factors included treatment with heparin and hemorrhagic accident with severe anemia. Relevant concurrent diseases included breast cancer (ongoing), hyperlipidemia, diabetes mellitus and hypertension. The patient was not exposed to any other erythropoietin-stimulating agent (ESA). Concomitant medication included heparin (dose and route of administration not reported) for thigh hematoma. Date of first dose of Retacrit was on 26-Oct-2012. Dose was 4000 with frequency of 1/week. It was reported that dose of Retacrit was not changed within 3 months prior to the event. Last dose of epoetin zeta prior to adverse events was received by the patient on an unknown day in Mar 2013. On 29-Mar-2013 at 06h45, leucocytes was at 9.735/mm3 (ref: 4.000-10.000), erythrocytes at 2,095,000/mm3 (ref: 4000000-5200000), hemoglobin at 6.3 g/dl (ref: 12.5-15.5), and hematocrit at 19.5% (ref: 37.0-47.0). On 06-Apr-2013 at 10h35, leucocytes was at 5.33 Giga/L (ref: 4-10), erythrocytes at 3.08 Tera/L (ref: 4.0-5.4), hemoglobin at 9.1 g/100 mL (ref: 12.01-16.4), and hematocrit at 29.5%. On 29-Mar-2013, the patient was hospitalized due to thigh hematoma and was put under heparin treatment (Hb: 6.3 g/dl). Transfusion was done (Hb: 9.1 g/dl). On 08-Apr-2013, a few days after, the patient experienced hemiplegia (stroke accident probable). Reaction was also reported as life threatening. The reporter's causality assessment for the event of fatal stroke accident in relation to epoetin zeta was not related. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product: batch number and date of expiry.

Case Comment: Overall case causality: Not assessable Based on the description of the events, it seems that these are more likely due to the sequelae arising from the medication error involving an anticoagulant, rather than epoetin, but cannot make a definitive assessment without further objective clinical event details, medical history and concomitant medications. - N. Gonzales (24 April 2013) Follow-up (02 Jun 2013) New information noted. Overall case and company causality changed to not related as the stroke was temporally related and sequelae to the heparin treatment and not to epoetin. - N. Gonzales

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	29-MAR-2013	Haematocrit	19.5 %	47.0 37.0
2	06-APR-2013	Haematocrit	29.5 %	47.0 37.0
3	29-MAR-2013	Haemoglobin	6.3 g/dl	15.5 12.5
4	06-APR-2013	Haemoglobin	9.1 g/100 mL,Unknown	16.4 12.0
5	29-MAR-2013	Red blood cell abnormality	2,095,000 /mm3	5200000 4000000
6	06-APR-2013	Red blood cell count	3.08 Tera/L,Unknown	5.4 4.0
7	29-MAR-2013	White blood cell count	9.735 /mm3	10 4
8	06-APR-2013	White blood cell count	5.33 Giga/L,Unknown	10 4

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();

Mfr. Control Number: 1685920

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		Allergies, alcohol consumption, tobacco usage, and medical history were not reported. The patient died on 10-Apr-2013. Causes of death were hemorragic accident of anticoagulant medication and stroke. It was not reported if an autopsy was performed. 21-May-2013: Follow-up information received from the investigator. Follow-up report created to reflect additional information regarding medical history. The patient has no history of smoking. The patient was not exposed to any other erythropoietin-stimulating agent (ESA). Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Anemia (Anaemia);
Unknown	Relevant Med History Risk Factor	Hemorrhagic stroke (Haemorrhagic stroke);
Unknown	Relevant Med History Risk Factor-BMI 37.4 g/m2; continuously	Obesity (Obesity);
Unknown	Relevant Med History Risk Factor	Anticoagulant therapy (Anticoagulant therapy);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	15	OCT	1933	78 Years	Male	85.00 kg	24	JUL	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Right ventricular failure [Right ventricular failure]
pulmonary embolism [Pulmonary embolism]
postinfarct [Infarction]
Pons infarct [Cerebral infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 26-JUL-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 25 IU/kg, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 27-OCT-2011 / 20-JUL-2012

19. THERAPY DURATION
#1) 268 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)
	Which led to the diagnosis of renal failure on 2010	
2010 to Ongoing	Relevant Med History	Renal failure (Renal failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1793228

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-JUN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up CIOMS I or MedWatch report may indicate in the appropriate field that it is an initial report.

Fatal right ventricular failure and postinfarct. Epoetin zeta. Hospira-sponsored study report, received from an investigator (reference: Ge-083-0006) which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post-Authorisation Safety Cohort Observation (PASCO II) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history included hypertensive nephropathy which led to the diagnosis of renal failure on 2010. It was reported that the patient was not on dialysis. The patient was not at any time exposed to any other erythropoietin-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications were not reported.
On 27-Oct-2011, the patient started treatment with epoetin zeta (Retacrit; subcutaneous; 25 IU/kg/week, 1 dose per week, lot number unknown) for renal anaemia. On an unknown date, the patient experienced right ventricular failure and postinfarct. The patient's visit date was reported as 25-Sep-2012. Investigations including examinations, laboratory, and diagnostic data, action taken with suspect drug, and treatment for the event of postinfarct were not reported. The patient recovered from the event of postinfarct on an unknown date. On 26-Jul-2014, the patient died. Cause of death was right ventricular failure. It was unknown if an autopsy was performed. The reporter's causality assessment between the event of right ventricular failure and epoetin zeta was not related while not reported for postinfarct. Hypertension was considered a risk factor.
21-Apr-2015: Additional information received from the same reporter. Death was added as adverse event. Additional information was also received regarding the patient's birth date, age, gender, ethnicity, height and weight, medical history, risk factor; dose, frequency, and therapy start date of suspect drug. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number, date of expiry and previous exposure of patient to other biosimilars.
08 Jun 2015: Corrected report has been created to change event seriousness assessment of the adverse event thromboembolic events from non-serious to serious (medically significant). This information has been incorporated in the narrative and corresponding data fields. 24 Aug 2015: Additional information was received from the same reporter. The event of thromboembolic events was updated to postinfarct, with an outcome of recovered. This information has been incorporated in the narrative and in corresponding data fields.
18-Nov-2015: Additional information was received from the same reporter. Cause of death was updated to right ventricular failure (previously unknown). This information has been incorporated in the narrative and in corresponding data fields.

Follow-up (25May2016): This is a follow-up report from a non-interventional study for Protocol EPOE-09-11, regarding subject 0830006. The investigator reported the subject received epoetin zeta (RETACRIT) subcutaneously once weekly from 27Oct2011 to 20Jul2012. Test data included hemoglobin: 7.695 moll. It was reported that the patient did not experience any thromboembolic event during treatment with any other ESA. There was no risk factor regarding: obesity (BMI 28.7), smoking, recent surgery, trauma, significant and short term weight changes due to fluid retention/excretion, aneurysm, immobilization, recent pregnancy, positive family history. Risk factors (start dates unknown) included: vascular anomalies, arterial hypertension, cerebral microangiopathy. The following were considered not relevant concurrent and past diseases of the patient: hyperlipidemia, transient ischemic attack, diabetes mellitus, atrial fibrillation, cancer (unspecified), chronic gastrointestinal disease, diarrhea, other unspecified diseases. With regard to relevant concurrent and past diseases of the patient: hypertension (start date unknown). Diagnosis of ponsinfarct, start date: 24Jul2012, stop date: 14Aug2012 was additionally reported. It was confirmed that the patient was not admitted to a hospital because of the adverse event. The event was not considered to be life threatening. The patient recovered on an unspecified date. No seriousness criteria was reported by the investigator for the event of pons-infarct. Additionally, the investigator reported the thromboembolic event pulmonary embolism which occurred on 25Jul2014 (patient died 26-Jul-2014) and stated that the event occurred very close to this. No seriousness criteria was reported for the event of pulmonary embolism. The action taken with the study medication in response to the event was not reported.
The investigator reported that the event of ponsinfarct was not related to treatment with epoetin zeta. The investigator did not provide causality for the event of pulmonary embolism

Follow-up (28Jun2016): This is a follow-up report from a non-interventional study for Protocol EPOE-09-11, regarding subject 0830006. New information received from the investigator via targeted questionnaire for Retacrit and thromboembolic events included: The subject did not receive any dialysis, new value for BMI and haemoglobin were provided, relevant risk factors included vascular anomalies, arterial hypertension and cerebral microangiopathia. Start and stop date of the event pulmonary embolism was reported. The patient was not admitted to hospital. Outcome was provided as fatal. Patient died on 26Jul2016. The event pulmonary embolism was assessed as unrelated to the study drug.

Follow-up (08Aug2016): Follow-up attempts completed. No further information expected. Case closed.

Case Comment: The right ventricular failure is unlikely related as patient had preexistent hypertension. The post-infarct still cannot be assessed without further objective clinical event details, including timing, location and description of the infarction.

Pons infarct is considered as possibly related to the use of epoetin zeta considering the known safety profile. Pulmonary embolism is considered as unrelated to the use of epoetin zeta due to the lack of a plausible temporal association.

Mfr. Control Number: 1793228

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The Follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body mass index	28.7	
2		Body mass index	27.6	
3		Haemoglobin	7.075	
4		Haemoglobin	7.695	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History Risk factor Arterial hypertension	Hypertension (Hypertension);
Unknown	Relevant Med History Risk factor	Vascular anomaly NOS (Vascular malformation);
Unknown	Relevant Med History Risk factor	Cerebral microangiopathy (Cerebral microangiopathy);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History Unspecified	Cancer (Neoplasm malignant);
Unknown	Relevant Med History	Gastrointestinal disorder (Gastrointestinal disorder);
Unknown	Relevant Med History	Diarrhoea (Diarrhoea);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	20	AUG	1935	78 Years	Male	74.66 kg	30	JAN	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplexia [Cerebrovascular accident]

Case Description: This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal apoplexia.
This serious case from an investigator (ref: Ge-012-0017) describes a 78-year-old male patient (weight: 74.66 kg and height: 176 cm) who received Retacrit (epoetin zeta; subcutaneous, dose, frequency, and batch number not reported) for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 30-JAN-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, Freq: 2 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-JUN-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History 1998	Coronary heart disease (Coronary artery disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1891763

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-SEP-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1891763

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

renal anaemia on an unknown date. Medical history included hyperlipidemia since 2005, coronary heart disease since 1998, and aortic valve replacement on Dec-2012. The patient was not previously exposed to any other erythropoetinstimulating agent. Concomitant medications were not reported. On an unknown date, the patient received epoetin zeta. On an unknown date, the patient was hospitalised due to endocarditis. On 30-Jan-2013, the patient experienced apoplexia as a result of cerebral infarction. Action taken with epoetin zeta and treatment for the adverse event were not reported. The patient died on 30-Jan-2013. Cause of death was apoplexia. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal apoplexia in relation to epoetin zeta was not assessable. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dose, batch number, and date of expiry. 11-Sep-2013: Follow-up information received from the same reporter. Follow-up report created to reflect new information regarding suspect drug and reporter's causality assessment. On 01-Jun-2011, the patient started treatment with epoetin zeta (3000 IE, 2 per week, batch number unknown). The reporter's causality assessment for the event of fatal apoplexia in relation to epoetin zeta was not related. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and date of expiry.

Case Comment: Overall case causality: Not assessable Canot provide event causation without further objective clinical event details, firm timeline of drug administration, medical history and pertinent laboratory results. - N. Gonzales (10 Sep 2013)
Follow-up: New information noted. Causality changed to not related. Noting an investigator causality of not related, patient age and cardiovascular risk factor (hyperlipidemia), consider the apoplexy to be due to natural pathophysiology of the reported condition. - N. Gonzales (16 Sep 2013)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption and tobacco usage were not reported. Medical history included hyperlipidemia since 2005, coronary heart disease since 1998, and aortic valve replacement on Dec-2012. The patient was not previously exposed to any other erythropoetin-stimulating agent. Race/Ethnicity: Caucasian. The patient died on 30-Jan-2013. Cause of death was apoplexia. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Endocarditis (Endocarditis);
Unknown to Ongoing	Relevant Med History 2005	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History Dec-2012	Aortic valve replacement (Aortic valve replacement);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	09	SEP	1964	48 Years	Male	163.00 kg	26	SEP	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombosis central venous catheter [Thrombosis in device]

Case Description: Fatal thrombosis central venous catheter. Epoetin zeta. Serious Hospira sponsored clinical study report from Germany, received from an investigator (reference: Ge-012-0022) which refers to a 48-year-old male patient (weight: 163.06 kg
and height: 170 cm). Medical history included hyperlipidemia, diabetes mellitus, hypertension, dyspnea, adiposides (all started on an unknown date in 2011), terminal dialysis-dependent kidney failure associated with questionable diabetic

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 16-NOV-2012
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 5000 IU, Freq: 3 Week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 01-JUN-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History 2011	() Adiposis (Obesity)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1891768

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-NOV-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

nephropathy and insertion of AV shunt on an unknown day in Apr-2012 with 2 adjustments in Aug-2012, diabetic foot syndrome (DFS) with s/p metatarsal V resection of the left foot, diabetic retinopathy, diabetic polyneuropathy (PNP), moderate peripheral artery disease (PAD), sleep apnoea syndrome with chronic obstructive pulmonary disease (COPD), extreme obesity, suspected secondary hypertension, moderate diverticulosis, and s/p staphylococcal sepsis. The patient was a smoker. The patient was not exposed to any other erythropoetin-stimulating agent. Concomitant medications were not reported. This patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. On 01-Jun-2011, the patient began treatment with Retacrit (epoetin zeta, 34/IU/kg/week also reported 5000 IE/3 week, twice a week, subcutaneous; lot number not reported) for renal anaemia. On 26-Sep-2012, the patient was hospitalized and developed thrombosis central venous catheter. On an unknown day in Sep-2012, the patient had a shunt because of suspected CVC infection. During the operation, cardiac arrest with resuscitation was noted. Action taken with the suspect drug and outcome of the adverse event were not reported. It was also reported that the patient was hospitalised from 14-Nov-2012 to 16-Nov-2012. Admission of the patient took place based on an intraoperative apparent circulatory instability. Surgical shunt insertion was scheduled based on dialysis dependent renal failure and existing atrial catheter with suspected catheter infection. Over the course of the operation, the patient experienced circulatory instability and was catecholamine-dependent; as a consequence, the surgery needed to be terminated and relocation to ITS took place. With relocation, the patient continued to appear catecholamine-dependent, was bradycardic and ultimately required resuscitation. After successful resuscitation, transesophageal echocardiography was performed on an unknown date. This indicated a pronounced right ventricular load and significant left ventricular hypovolaemia. With pronounced mixed acidosis and hyperkalaemia, dialysis via a Shaldon catheter was performed in parallel. Under dialysis, sedation and invasive ventilation, the patient's condition remained stable at a low level. However, the patient continued to be catecholamine-dependent and required resuscitation two more times. In the context of the clinical examinations, a persistent mydriasis became apparent as well as anisocoria. On an unknown date, neurological consultation was held. This suggested suspected severe hypoxic brain damage. A fulminant increase in transaminase with slightly compromised coagulation was apparent; a sonograph indicated no morphological abnormalities of the liver. Transaminases regressed in follow-up examinations. With suspicion of a septic event, administration of antibiotics (vancomycin and ertapenem; doses and routes of administration not reported) was done. A sonograph revealed no evidence of septic infarction of the spleen, as far as poor imaging allowed. Thus, an abdominal CT and CCT upon suspicion of hypoxic brain damage were planned. The CCT indicated pronounced cerebral oedema with transtentorial herniation which warranted further diagnostic investigation to be abstained. The patient was no longer able to be stabilised. On 16-Nov-2012, the patient died. Cause of death was thrombosis central venous catheter. Post-mortem examination indicated cardiac failure associated with biventricular cardiac decompensation and CHD with high grade stenosis of the LAD as the cause of death. A peripheral left pulmonary embolism presented the aspect of a prior embolism, such that acute cardiac failure was not necessarily attributable. The cause for the impaired coagulation is likely disrupted synthesis associated with steatosis hepatis. There was no evidence of a septic event except an enlargement of the spleen, although there was no inflammatory lesion or septic organ embolism. As far as the renal failure, macroscopic evidence suggested suspicion of glomerulonephritis and an additional histological preparation will follow. In addition, histological samples of cerebral tissue will follow. Secondarily, there was a right adrenocortical adenoma, meaning secondary hypertonus cannot be ruled out. The reporter's causality assessment for the event of fatal thrombosis central venous catheter in relation to epoetin zeta was not assessable. 11-Sep-2013: Additional information was received from the same reporter. Follow up was created to reflect new information, dose and frequency of epoetin zeta was added; the reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number. This information has been incorporated in the narrative and in the corresponding data fields. 16-Sep-2013: English translation of the discharge letter was received. Follow up report was created to reflect details regarding event. Terminal dialysis-dependent kidney failure, diabetic nephropathy, insertion of AV shunt, diabetic foot syndrome (DFS), diabetic retinopathy, diabetic polyneuropathy (PNP), moderate peripheral artery disease (PAD), sleep apnoea syndrome with chronic obstructive pulmonary disease (COPD), extreme obesity, suspected secondary hypertension, moderate diverticulosis, and s/p staphylococcal sepsis were added as medical history. Laboratory and diagnostic tests were added; autopsy result was provided. Data entry correction was also made regarding patient's detail. The patient's birthdate was updated; age was changed to 48 years. Cause of death was updated to cardiac failure (previously reported as coronary heart disease). This information has been incorporated in the narrative and in the corresponding data fields. 28-Mar-2014: Corrected report was created to add the event fatal sepsis. 04-Apr-2014: Additional information was received from the investigator and confirmed that there was no septic adverse event. 26-Nov-2014: Additional information was received from the same reporter. Follow-up report was created to reflect new information that cause of death of patient was thrombosis in central venous catheter. Therapy start date and history of smoking were also added. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Not assessable Although the suspect drug can theoretically lead to thrombosis in general, cannot provide a definite causation without further objective clinical event details and concomitant medications. Consider also possible contributory effects of how the catheter site was being managed. - N. Gonzales (10 Sep 2013) Follow-up: No change in previous assessment. - N. Gonzales (16 Sep 2013) Follow-up: New information received on the course of the patient leading to death. Deterioration of condition is due to progression and complications of preexistent medical conditions. Still cannot provide causality on the device thrombosis as this is multifactorial in nature. - N. Gonzales (20 Sep 2013) Follow-up (01 Apr 2014): No change in assessment for previous event. Sepsis is also not assessable.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Cannot provide event causation without objective clinical event results. - R. Jacot Follow-up (17 Apr 2014): No change in previous company assessment. - R. Jacot Follow-up: No change in previous assessment. - N. Gonzales (04 Dec 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Echocardiogram	Right ventricular load, unk	
2		Echocardiogram	Significant left ventricular hypovolaemia, unk	
3		Transaminases	Fulminant increase, unk	
4		Transaminases	Regressed, unk	
5		Ultrasound scan	No morphological abnormalities of the liver, unk	
6		Ultrasound scan	No evidence of septic infarction of the spleen	

13. Relevant Tests

CCT- CT brain scan- Result- Cerebral oedema with transtentorial herniation, unk
Sonograph- Sonogram- Result- No evidence of septic infarction of the spleen, unk

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies were not reported. Medical history included hyperlipidemia, diabetes mellitus, hypertension, dyspnea, adiposides (all started on an unknown date in 2011), terminal dialysis-dependent kidney failure associated with questionable diabetic nephropathy and insertion of AV shunt on an unknown day in Apr-2012 with 2 adjustments in Aug-2012, diabetic foot syndrome (DFS) with s/p metatarsal V resection of the left foot, diabetic retinopathy, diabetic polyneuropathy (PNP), moderate peripheral artery disease (PAD), sleep apnoea syndrome with chronic obstructive pulmonary disease (COPD), extreme obesity, suspected secondary hypertension, moderate diverticulosis, and s/p staphylococcal sepsis. The patient was a smoker. The patient was not exposed to any other erythropoetin-stimulating agent. On 16-Nov-2012, the patient died. Cause of death was thrombosis central venous catheter. Risk factor included diabetes and smoking. Post-mortem examination indicated cardiac failure associated with biventricular cardiac decompensation and CHD with high grade stenosis of the LAD as the cause of death. A peripheral left pulmonary embolism presented the aspect of a prior embolism, such that acute cardiac failure was not necessarily attributable. The cause for the impaired coagulation is likely disrupted synthesis associated with steatosis hepatis. There was no evidence of a septic event except an enlargement of the spleen, although there was no inflammatory lesion or septic organ embolism. As far as the renal failure, macroscopic evidence suggested suspicion of glomerulonephritis and an additional histological preparation will follow. In addition, histological samples of cerebral tissue will follow. Secondarily, there was a right adrenocortical adenoma, meaning secondary hypertonus cannot be ruled out. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Anisocoria (Pupils unequal);
Unknown to Ongoing	Relevant Med History	COPD (Chronic obstructive pulmonary disease);
Unknown to Ongoing	Relevant Med History	Diabetic foot (Diabetic foot);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Diabetic polyneuropathy (Diabetic neuropathy);
Unknown to Ongoing	Relevant Med History	Diabetic retinopathy (Diabetic retinopathy);
Unknown to Ongoing	Relevant Med History 2011	Dyspnea (Dyspnoea);
Unknown to Ongoing	Relevant Med History	Morbid obesity (Obesity);
Unknown to Ongoing	Relevant Med History 2011	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History 2011	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History Terminal dialysis dependent	Kidney failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Diverticulosis (Diverticulum);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Mydriasis (Mydriasis);
Unknown to Ongoing	Relevant Med History	Adrenocortical carcinoma (Adrenocortical carcinoma);
Unknown to Ongoing	Relevant Med History	Secondary hypertension (Secondary hypertension);
Unknown to Ongoing	Relevant Med History	Sleep apnoea syndrome (Sleep apnoea syndrome);
Unknown to Ongoing	Relevant Med History	Steatosis hepatic (Hepatic steatosis);
Unknown	Relevant Med History	Arteriovenous shunt placement (Arteriovenous fistula operation);
Unknown	Relevant Med History	Foot surgery (Foot operation);
Unknown	Relevant Med History	Staphylococcal sepsis (Staphylococcal sepsis);
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown	Relevant Med History	Smoker (Tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	24	JAN	1970	43 Years	Male	80.20 kg	28	AUG	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart attack [Myocardial infarction]

Case Description: This is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). This report from Germany describes a case of fatal heart attack. This serious
case from an investigator (reference: Ge-027-0028) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency, and batch number not reported) for renal anaemia on an unknown

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 03-SEP-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3 x 2000 I (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-DEC-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACTRAPID /00646001/ (INSULIN HUMAN) ; Unknown
#2) DIOVAN (VALSARTAN) Tablet ; Unknown
#3) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHE
#4) FERMED /00023550/ (SACCHARATED IRON OXIDE) ; Unknown
#5) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX) ; Unknown
#6) LEVEMIR (INSULIN DETEMIR) Solution for injection in pre-filled syringe ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Left ventricular ejection fraction (Ejection fraction)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1897663

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-OCT-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

date. Medical history and concomitant medications were not reported. On an unknown date, the patient started treatment with epoetin zeta and experienced heart attack. Treatment for the adverse event and action taken with the suspect drug were not reported. The patient died on 03-Sep-2013. Cause of death was heart attack. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal heart attack in relation to the study medication epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered, batch number, date of expiry, previous exposure of patient to other biosimilars. 15-Sep-2013: Follow-up information received from the investigator. Follow-up report created to reflect new information regarding medical history and reporter's causality assessment. Medical history included two heart infarctions and coronary heart disease. The reporter stated that there was no relation between the fatal heart attack and the medication with Retacrit. 30-Sep-2013: Follow-up information was received from the investigator. Follow-up report created to reflect new information regarding patient details, seriousness criteria, suspect drug, adverse event, and medical history. Seriousness criteria of life threatening and hospitalisation were added. The reporter was able to provide the following for identification and traceability of the biosimilar product epoetin zeta: dosage administered and previous exposure of patient to other biosimilars. The patient was a 43-year-old male (dry weight: 80.2 kg). Medical history included hemodialysis, obesity since childhood, smoking, anterior myocardial infarction PTCA with stent in 1999, NSTEMI RCA PTCA with stent on an unknown day in Jun-2009, diabetes mellitus type I since an unknown day in Jun-1980, hyperlipidemia, ischemic heart disease, hypertension, COPD, and positive family history (brother died of the same cause). From an unknown date (also reported as <8.2009) until 03-Jun-2011, the patient was exposed to other erythropoetin-stimulating agent NeoRecormon (mean dose 3000; unit and route of administration not reported) given for an unknown indication. The patient did not experience any thrombolic event during treatment with any other erythropoetin-stimulating agent. The patient started treatment with epoetin zeta (3 x 2000 IE, 3 times a week) on 01-Dec-2011. The last dose prior to the event was given on 27-Aug-2013. On 28-Aug-2013, the patient experienced myocardial infarction and was admitted to the hospital. On the same day, the patient was asystolic and CPR was performed. The reporter was unable to provide the following for identification and traceability of the biosimilar product epoetin zeta: batch number. 07-Oct-2013: English translation of the German text from the investigator was received. Follow up report created to reflect additional information regarding suspect drug, medical history, concomitant medications, laboratory data, and adverse events. Route of administration of Retacrit was reported as intravenous. The patient received Retacrit 2000 IU/0.6 ml injection solution ready-to-use syringe on Tuesdays, Thursdays and Saturdays for dialysis. Formulations of Retacrit were 2000 IU/0.6 ml inj. sol. ready-to-use syringe 6 units FER (given on 23-Jul-2013, 13-Jul-2013, 25-Jun-2013 and 06-Apr-2013) and 3000 IU/0.9 ml inj. sol. ready-to-use syringe 6 units FER, which was reported as discontinued on an unknown date. Formulations of NeoRecormon were reported as 3000 IU, 4000 IU, 5000 IU, and 10000 IU ready-to-use-syringes 6 units FER. Concomitant medications included Novaminsulfon Ratiopharm 500 mg tablets (up to 4 x 2 tablets; route of administration not reported) for pain; Movicol powder sachets for constipation, glucagon hypokit dry matter with solution for severe hypoglycaemia (doses and routes of administration not reported); ASA 100 1 A pharma tablets (1-0-0-0), metoprolol 100 retard 1A pharma tablets (0-0-1/2-0), simvastatin Krewel 40 mg coated tablets (0-0-1-0), Dreisavit N coated tablets (0-0-1-0), anti potassium NA granulate sachet following a potassium rich meal, Levemir FlexPen ready-to-use syringe (12-0-16-0), Actrapid Penfill 100 IU/ml injection solution incartridge (according to blood sugar), Spiriva 18 mcg capsules with inhalation refill unit (1-0-0-0), salbutamol Ratiopharm N 3x200 inhaler dose aer. (up to 6 puffs per day), Osvaren coated tablets (3-3-3-0, 1 additional between meals), calcitriol GRY 0.5 mg capsules (1-0-0-0), Valsartan Hormosan Pharma 80 mg coated tablets (diovan, 0-0-1-0), L-thyroxin beta 200 mcg tablets (1-0-0-0), Ferrlecit 62.5 mg ampoules 6x5 ml AMP (dose not reported), and Vanco Saar 500 mg vials 6 units DFL (dose not reported); routes of administration not reported) all given for unknown indications. For dialysis, the patient was given Nefrocarnit ampoules 10 units AMP (1g, weekly dose of 1g; intravenous) and Fermed ampoules 5 x 5 ml AMP (100 mg, weekly doses of 8.33 mg then 200 mg, weekly interval 12; intravenous). Stent insertion in 1999 was described as stent implant of the LAD, hypertension was specified as pulmonary hypertension and arterial hypertension, COPD was reported as stage II. History of smoking was described as chronic nicotine abuse. On an unknown day in May-2009, the patient underwent shunt insertion left forearm (Cimino shunt). It was reported that the patient had haemodialysis since 19-Jun-2009. NSTEMI RCA was described as occlusion of the Ramus circumflexus (BM in the Ramus circumflexus multiple times). Also on an unknown day in Jun-2009, the patient was also s/p resuscitation (also reported as CPR) following cardiogenic shock and intra-aortic balloon counterpulsation. Medical history also included dialysis-dependent terminal kidney disease, bilateral pneumonia, ventricular tachycardia, and ventricular fibrillation in Jun-2009. On 18-Jun-2013 at 07:28:00, laboratory results included pH of 7.45, BE of 5.3 mmol/l, HCO3 of 29 mmol/l, SO2 of 96%, pO2 of 79 mmHg, pCO2 of 43 mmHg, HCO3- of 29.9 mmol/l (reference ranges not reported). On 25-Jun-2013 at 07:25:00, laboratory data showed pH of 7.44, BE of 3.9 mmol/l, HCO3 of 28 mmol/l, SO2 of 96%, pO2 of 77 mmHg, pCO2 of 42 mmHg, HCO3- of 28.5 mmol/l. The patient had a known 3-vessel coronary disease with reduced left ventricular function EF ca 30%. The patient also had diabetic nephropathy, diabetic retinopathy, insulin pump therapy, secondary renal hyperparathyroidism, chronic heart failure also reported as cardiac insufficiency NYHA II-III, mitral valve insufficiency II-III in Jul-2009, and hyperthyroidism (also reported as hypothyroidism) associated with Hashimoto's thyroiditis. In addition, the patient had cataract, s/p surgery both eyes, hyperuricaemia, suspected aspiration pneumonia, chronic constipation under phosphate binder therapy, suspected sinobronchial syndrome, sinusitis, metabolic syndrome, hepatitis B - vaccination failure, and hypokalaemia. It was also reported that the patient had a history of non-compliance. On 02-Jul-2013, investigations revealed haematocrit of 32.5% (normal range: 42.0-54.0), haemoglobin of 10.9 g/dl (normal range: 13.0-18.0), and creatinine of 8.11 mg/dl (normal value: less than 1.3). On the same day at 07:28:00, laboratory data showed pH of 7.44, BE of 1.6 mmol/l, HCO3 of 26.1 mmol/l, SO2 of 93%, pO2 of 65 mmHg, pCO2 of 38 mmHg, HCO3- of 25.8 mmol/l. On 09-Jul-2013 at 07:27:00,

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

laboratory results included pH of 7.45, BE of 4.7 mmol/l, HCO3 of 28.6 mmol/l, SO2 of 97%, pO2 of 86 mmHg, pCO2 of 42 mmHg, HCO3- of 29.2 mmol/l. On 11-Jul-2013, the patient had bronchitis with yellow discharge and cefpodoxime (1A Pharma, Dura, Ratiopharm) 200 mg coated tablets 10 units FTA (200 mg, route of administration not reported) was prescribed. On 16-Jul-2013 at 07:29:00, investigations showed pH of 7.48, BE of 5.9 mmol/l, HCO3 of 29.5 mmol/l, SO2 of 96%, pO2 of 77 mmHg, pCO2 of 40 mmHg, HCO3- of 29.8 mmol/l. On 23-Jul-2013 at 07:20:00, laboratory data included pH of 7.47, BE of 3.9 mmol/l, HCO3 of 28 mmol/l, SO2 of 96%, pO2 of 74 mmHg, pCO2 of 38 mmHg, HCO3- of 27.7 mmol/l. On 30-Jul-2013 at 07:40:00, laboratory results showed pH of 7.48, BE of 3.5 mmol/l, HCO3 of 27.7 mmol/l, SO2 of 99%, pO2 of 118 mmHg, pCO2 of 36 mmHg, HCO3- of 26.8 mmol/l. On 06-Aug-2013 at 07:24:00, laboratory data included pH of 7.45, BE of 2.3 mmol/l, HCO3 of 26.6 mmol/l, SO2 of 90%, pO2 of 56 mmHg, pCO2 of 38 mmHg, HCO3- of 26.4 mmol/l. On 13-Aug-2013 at 07:25:00, investigations revealed pH of 7.48, BE of 5.9 mmol/l, HCO3 of 29.5 mmol/l, SO2 of 96%, pO2 of 78 mmHg, pCO2 of 40 mmHg, HCO3- of 29.8 mmol/l. On 20-Aug-2013, laboratory result included haematocrit of 31%, haemoglobin of 10.7 g/dl, creatinine of 7.99 mg/dl, LDL cholesterol of 56 mg/dl (normal value: less than 160), HDL of 40 mg/dl (normal value: greater than 40), cholesterol of 114 mg/dl (normal value: less than 200), and triglyceride of 88 mg/dl (normal value: less than 150). On the same day at 07:26:00, laboratory data showed pH of 7.48, BE of 5.9 mmol/l, HCO3 of 29.5 mmol/l, SO2 of 94%, pO2 of 66 mmHg, pCO2 of 40 mmHg, HCO3- of 29.8 mmol/l. It was reported that Fermed was increased on 22-Aug-2013. On 27-Aug-2013 at 07:32:00, further investigations revealed pH of 7.47, BE of 6.3 mmol/l, HCO3 of 29.9 mmol/l, SO2 of 98%, pO2 of 103 mmHg, pCO2 of 42 mmHg, HCO3- of 30.6 mmol/l. It was reported that the patient was admitted to the hospital following successful resuscitation associated with an asystole in conjunction with NSTEMI (at home) on 28-Aug-2013. It was stated that third party anamnesis (mother) provided unclear information about the duration the patient was down prior to resuscitation. On an unknown date, neurological examination following CPR indicated round pupils, left eye opaque, right eye non-responsive, average width. Because there was haemodynamic instability despite catecholamine (unspecified) treatment and no evidence of ST elevation myocardial infarction, invasive cardiological investigation was avoided for the polymorbid patient with known far advanced ongoing previous findings (2009) of non-revascularizable CHD. On 28-Aug-2013, the patient was intubated and ventilated under analgesic sedation (unspecified). Due to suspected hypoxic brain damage, a CCT examination and testing of NSE values were performed. On 30-Aug-2013, CCT exam indicated no evidence of cerebral oedema and no ICB or disruption to CSF circulation. On an unknown date, the NSE value was elevated at 46.2 mcg/l (reference range not reported). It was stated that regular dialysis was carried out due to terminal renal failure (Tues, Thurs, Sat). On 03-Sep-2013, the patient developed circulatory instability and also did not respond well to high-dose catecholamine treatment. On an unknown date, it was also reported that intensified treatment (unspecified) was unsuccessful. Cause of death was also reported as acute cardiac failure.

Case Comment: Overall case causality: Not assessable Cannot provide causation without firm timeline, objective clinical event details, firm timeline, pertinent laboratory results, medical history and concomitant medications. - N. Gonzales (15 Sep 2013) Follow-up: New information noted. Causality changed to not related as patient had previous history of myocardial infarction and coronary artery disease. - N. Gonzales (20 Sep 2013) Follow-up: No change in previous assessment. - N. Gonzales (05 Oct 2013) Follow-up: No change in previous assessment. - N. Gonzales (11 Oct 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	18-JUN-2013	Base excess	5.3 mmol/l	
2	25-JUN-2013	Base excess	3.9 mmol/l	
3	02-JUL-2013	Base excess	1.6 mmol/l	
4	09-JUL-2013	Base excess	4.7 mmol/l	
5	16-JUL-2013	Base excess	5.9 mmol/l	
6	23-JUL-2013	Base excess	3.9 mmol/l	
7	30-JUL-2013	Base excess	3.5 mmol/l	
8	06-AUG-2013	Base excess	2.3 mmol/l	
9	13-AUG-2013	Base excess	5.9 mmol/l	
10	20-AUG-2013	Base excess	5.9 mmol/l	
11	27-AUG-2013	Base excess	6.3 mmol/l	

Mfr. Control Number: 1897663

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
12	18-JUN-2013	Blood bicarbonate	29.9 mmol/l	
13	18-JUN-2013	Blood bicarbonate	29 mmol/l	
14	25-JUN-2013	Blood bicarbonate	28.5 mmol/l	
15	25-JUN-2013	Blood bicarbonate	28 mmol/l	
16	02-JUL-2013	Blood bicarbonate	25.8 mmol/l	
17	02-JUL-2013	Blood bicarbonate	26.1 mmol/l	
18	09-JUL-2013	Blood bicarbonate	28.6 mmol/l	
19	09-JUL-2013	Blood bicarbonate	29.2 mmol/l	
20	16-JUL-2013	Blood bicarbonate	29.8 mmol/l	
21	16-JUL-2013	Blood bicarbonate	29.5 mmol/l	
22	23-JUL-2013	Blood bicarbonate	28 mmol/l	
23	23-JUL-2013	Blood bicarbonate	27.7 mmol/l	
24	30-JUL-2013	Blood bicarbonate	27.7 mmol/l	
25	30-JUL-2013	Blood bicarbonate	26.8 mmol/l	
26	06-AUG-2013	Blood bicarbonate	26.6 mmol/l	
27	06-AUG-2013	Blood bicarbonate	26.4 mmol/l	
28	13-AUG-2013	Blood bicarbonate	29.8 mmol/l	
29	13-AUG-2013	Blood bicarbonate	29.5 mmol/l	
30	20-AUG-2013	Blood bicarbonate	29.5 mmol/l	
31	20-AUG-2013	Blood bicarbonate	29.8 mmol/l	
32	27-AUG-2013	Blood bicarbonate	30.6 mmol/l	
33	27-AUG-2013	Blood bicarbonate	29.9 mmol/l	
34	20-AUG-2013	Blood cholesterol	114 mg/dl	
35	02-JUL-2013	Blood creatinine	8.11 mg/dl	
36	20-AUG-2013	Blood creatinine	7.99 mg/dl	
37	20-AUG-2013	Blood triglycerides	88 mg/dl	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
38	30-AUG-2013	Computerised tomogram head	No evidence of cerebral oedema Unknown	
39	30-AUG-2013	Computerised tomogram head	No ICB or disruption to CSF circulation Unknown	
40	02-JUL-2013	Haematocrit	32.5 %	54.0 42.0
41	20-AUG-2013	Haematocrit	31 %	54.0 42.0
42	02-JUL-2013	Haemoglobin	10.9 g/dl	18.0 13.0
43	20-AUG-2013	Haemoglobin	10.7 g/dl	18.0 13.0
44	20-AUG-2013	High density lipoprotein	40 mg/dl	
45	20-AUG-2013	Low density lipoprotein	56 mg/dl	
46		Neurological examination	Right eye non-responsive, average width Unknown	
47		Neurological examination	Round pupils, left eye opaque Unknown	
48		Neurone-specific enolase	Elevated at 46.2 MCG/L	
49	18-JUN-2013	Oxygen saturation	96 %	
50	25-JUN-2013	Oxygen saturation	96 %	
51	02-JUL-2013	Oxygen saturation	93 %	
52	09-JUL-2013	Oxygen saturation	97 %	
53	16-JUL-2013	Oxygen saturation	96 %	
54	23-JUL-2013	Oxygen saturation	96 %	
55	30-JUL-2013	Oxygen saturation	99 %	
56	06-AUG-2013	Oxygen saturation	90 %	
57	13-AUG-2013	Oxygen saturation	96 %	
58	20-AUG-2013	Oxygen saturation	94 %	
59	27-AUG-2013	Oxygen saturation	98 %	
60	18-JUN-2013	PCO2	43 mmHg	
61	25-JUN-2013	PCO2	42 mmHg	
62	02-JUL-2013	PCO2	38 mmHg	
63	09-JUL-2013	PCO2	42 mmHg	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
64	16-JUL-2013	PCO2	40 mmHg	
65	23-JUL-2013	PCO2	38 mmHg	
66	30-JUL-2013	PCO2	36 mmHg	
67	06-AUG-2013	PCO2	38 mmHg	
68	13-AUG-2013	PCO2	40 mmHg	
69	20-AUG-2013	PCO2	40 mmHg	
70	27-AUG-2013	PCO2	42 mmHg	
71	18-JUN-2013	PO2	79 mmHg	
72	25-JUN-2013	PO2	77 mmHg	
73	02-JUL-2013	PO2	65 mmHg	
74	09-JUL-2013	PO2	86 mmHg	
75	16-JUL-2013	PO2	77 mmHg	
76	23-JUL-2013	PO2	74 mmHg	
77	30-JUL-2013	PO2	118 mmHg	
78	06-AUG-2013	PO2	56 mmHg	
79	13-AUG-2013	PO2	78 mmHg	
80	20-AUG-2013	PO2	66 mmHg	
81	27-AUG-2013	PO2	103 mmHg	
82	18-JUN-2013	pH body fluid	7.45 Unknown	
83	25-JUN-2013	pH body fluid	7.44 Unknown	
84	02-JUL-2013	pH body fluid	7.44 Unknown	
85	09-JUL-2013	pH body fluid	7.45 Unknown	
86	16-JUL-2013	pH body fluid	7.48 Unknown	
87	23-JUL-2013	pH body fluid	7.47 Unknown	
88	30-JUL-2013	pH body fluid	7.48 Unknown	
89	06-AUG-2013	pH body fluid	7.45 Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
90	13-AUG-2013	pH body fluid	7.48 Unknown	
91	20-AUG-2013	pH body fluid	7.48 Unknown	
92	27-AUG-2013	pH body fluid	7.47 Unknown	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	3 x 2000 IE, Freq: 3 Week; Interval 1; Intravenous	Renal anemia (Nephrogenic anaemia)	01-DEC-2011 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHENATE, FOLIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) Tablet ; Unknown

#7) METOPROLOL 1A PHARMA (METOPROLOL TARTRATE) Tablet ; Unknown

#8) MOVICOL /01749801/ (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE) ; Unknown

#9) NEFROCARNIT (LEVOCARNITINE) ; Unknown

#10) NOVAMINSULFON-RATIOPHARM (METAMIZOLE SODIUM) Tablet ; Unknown

#11) OSVAREN (CALCIUM ACETATE, MAGNESIUM CARBONATE) Tablet ; Unknown

#12) SALBUTAMOL-RATIOPHARM N (SALBUTAMOL SULFATE) ; Unknown

#13) SPIRIVA (TIOTROPIUM BROMIDE) Capsule ; Unknown

#14) VANCO (VANCOMYCIN HYDROCHLORIDE) ; Unknown

#15) ANTI-KALIUM NA (SODIUM POLYSTYRENE SULFONATE) ; Unknown

#16) ASA (ACETYLSALICYLIC ACID) Tablet ; Unknown

#17) CALCITRIOL (CALCITRIOL) Capsule ; Unknown

#18) CEFPODOXIME (CEFPODOXIME) Tablet ; Unknown

#19) GLUCAGON (GLUCAGON) ; Unknown

#20) L-THYROXIN BETA (LEVOTHYROXINE SODIUM) Tablet ; Unknown

#21) SIMVASTATIN (SIMVASTATIN) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage, and medical history were not reported. 15-Sep-2013: Follow-up information received from the investigator regarding medical history. Medical history included two heart

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		infarctions and coronary heart disease. 30-Sep-2013: Follow-up information received from the investigator regarding medical history. Medical history included hemodialysis, obesity since childhood, smoking, anterior myocardial infarction PTCA with stent in 1999, NSTEMI RCA PTCA with stent on an unknown day in Jun-2009, diabetes mellitus type I since an unknown day in Jun-1980, hyperlipidemia, ischemic heart disease, hypertension, COPD, and positive family history (brother died of the same cause). From an unknown date (also reported as <8.2009) until 03-Jun-2011, the patient was exposed to other erythropoetin-stimulating agent NeoRecormon (mean dose 3000; unit and route of administration not reported) given for an unknown indication. The patient did not experience any thrombolic event during treatment with any other erythropoetin-stimulating agent. Race/Ethnicity: Caucasian 07-Oct-2013: Follow up information received from the same reporter to reflect additional information regarding medical history. Stent insertion in 1999 was described as stent implant of the LAD, hypertension was specified as pulmonary hypertension and arterial hypertension, COPD was reported as stage II. History of smoking was described as chronic nicotine abuse. On an unknown day in May-2009, the patient underwent shunt insertion left forearm (Cimino shunt). It was reported that the patient had haemodialysis since 19-Jun-2009. NSTEMI RCA was described as occlusion of the Ramus circumflexus (BM in the Ramus circumflexus multiple times) and PTCA with stent in Jun-2009 was described as intra-aortic balloon counterpulsation. Also on an unknown day in Jun-2009, the patient was also s/p resuscitation (also reported as CPR) following cardiogenic shock. -Cont...
Unknown to Ongoing	Relevant Med History	Triple vessel disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension);
Unknown to Ongoing	Relevant Med History Jun-2009	Bilateral pneumonia (Pneumonia);
Unknown to Ongoing	Relevant Med History NYHA II-III	Cardiac insufficiency (Cardiac failure);
Unknown	Relevant Med History Plus intra-aortic balloon counterpulsation	Cardiogenic shock (Cardiogenic shock);
Unknown to Ongoing	Relevant Med History	Constipation chronic (Constipation);
Unknown to Ongoing	Relevant Med History Stage II	COPD (Chronic obstructive pulmonary disease);
Unknown to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History Jun-1980	Type I diabetes mellitus (Type 1 diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Diabetic retinopathy (Diabetic retinopathy);
Unknown to Ongoing	Relevant Med History	End stage renal failure (End stage renal disease);
Unknown to Ongoing	Relevant Med History	Hepatitis B (Hepatitis B);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hashimoto's thyroiditis (Autoimmune thyroiditis);
Unknown to Ongoing	Relevant Med History	Hyperthyroidism (Hyperthyroidism);
Unknown to Ongoing	Relevant Med History	Hypothyroidism (Hypothyroidism);
Unknown to Ongoing	Relevant Med History	Hyperuricaemia (Hyperuricaemia);
Unknown to Ongoing	Relevant Med History	Hypokalaemia (Hypokalaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Metabolic syndrome (Metabolic syndrome);
Unknown to Ongoing	Relevant Med History NYHA II-III in Jul-2009	Mitral valve insufficiency (Mitral valve incompetence);
Unknown to Ongoing	Relevant Med History	Pulmonary hypertension (Pulmonary hypertension);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown to Ongoing	Relevant Med History	Sinusitis (Sinusitis);
Unknown to Ongoing	Relevant Med History	Aspiration pneumonia (Pneumonia aspiration);
Unknown to Ongoing	Relevant Med History	Sinobronchial syndrome (Sinobronchitis);
Unknown to Ongoing	Relevant Med History Jun-2009	Ventricular fibrillation (Ventricular fibrillation);
Unknown to Ongoing	Relevant Med History Jun-2009	Ventricular tachycardia (Ventricular tachycardia);
Unknown	Relevant Med History	Death of brother (Death of relative);
Unknown	Relevant Med History 1999	Anterior myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Cataract (Cataract);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History Jun-2009	Non STEMI (Acute myocardial infarction);
Unknown	Relevant Med History 1999 and Jun-2009	Coronary arterial stent insertion (Coronary arterial stent insertion);
Unknown	Relevant Med History 1999 and Jun-2009	Percutaneous transluminal angioplasty (Angioplasty);
Unknown	Relevant Med History	Cimino shunt (Arteriovenous fistula operation);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	May-2009	
Unknown	Relevant Med History	Cataract operation (Cataract operation);
Unknown	Relevant Med History	Nicotine abuse (Tobacco abuse);
Unknown	Relevant Med History Since 19-Jun-2009	Hemodialysis (Haemodialysis);
Unknown	Relevant Med History	Treatment noncompliance (Treatment noncompliance);
Unknown	Relevant Med History	Obesity (Obesity);
Unknown to 03-JUN-2011	Past Drug Event	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: No adverse event (No adverse event)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	19	DEC	1938	74 Years	Female	82.00 kg	22	MAY	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]
Subdural hematoma right [Subdural haematoma]
Basal ganglia hemorrhage right [Basal ganglia haemorrhage]

Case Description: Fatal subdural hematoma right, fatal basal ganglia hemorrhage right, lack of efficacy. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (ref: Ge-463-0008) describes a 74-year-old female Caucasian patient (height: 150 cm, dry weight: 82 kg). The patient had penicillin allergy.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [x] PATIENT DIED Date: 01-JUL-2014
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 48.60 iu/kg/week,0.5 dosage/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-MAR-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Diagnosed 01-Feb-1997	Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2021971

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-NOV-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included hyperlipidemia from 05-Apr-2011 until 01-Jul-2014, chemotherapeutics-induced renal failure; and was diagnosed of renal failure
on 01-Feb-1997. The patient was not on dialysis. The patient was not treated with an Erythropoiesis-Stimulating Agent (ESA) before the treatment with Retacrit, and she did not receive Retacrit prior the study. Concomitant medications were
not reported. This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. On 01-Mar-2013, the patient
received epoetin zeta (Retacrit; 48.6 IU/kg/week, subcutaneous, 0.5 dosage per week, lot number not reported; mean dose reported as 8000 unit of measurement not reported) for renal anaemia. On 22-May-2013, the monitor found in the
patient record that the patient's Hb was still too low which was thought to be a sign of lack of efficacy. On 22-May-2013, treatment was changed from Retacrit to darbepoetin alfa (Aranesp 50; dose and route of administration not reported;
mean dose reported as 50 unit of measurement not reported) as the site failed to check the iron value in the blood. This was probably resulted due to lack of efficacy of Retacrit. On unknown days from May until Oct-2013, Hb increased from
10.0 to 12.3 (unit and normal value not reported). It was also reported that due to the good Hb value, the patient did not receive epoetin at the moment but the report stated that the site will treat the patient again in case of falling Hb values.
Therapy end date for Aranesp was on 19-Oct-2015. On an unknown date, the patient experienced subdural hematoma right and basal ganglia hemorrhage right. However, it was reported that the patient did not experience any
thromboembolic event during the treatment with other ESA, Aranesp. On 24-Jun-2014, the patient was admitted due to moderate dementia. The patient was introduced by the emergency doctor. The reason for alerting the emergency
doctor was an increased worsening of the general state of health, in the sense of decreasing oxygenation and hypotonic blood pressure values, in the case of existing multimorbidity. On 26-Jun-2014, the patient became an inpatient.
Treatment diagnosis was large subdural haematoma right and basal ganglia bleeding right, midline relocation to the left; pneumonia right; status after allogenic kidney transplant (Mar-2004) with limited transplant function, terminal kidney
failure (Feb-1997), with primarily chemotherapy induced kidney failure; status after hysterectomy and adnexaectomy on both sides with subsequent polychemotherapy, with status after ovarian carcinoma left; arterial hypertension; diabetes
mellitus type 2, insulin dependent; hyperparathyroidism with parathyroid adenoma right; status after deep leg vein thrombosis right and relapse of thrombosis on right lower thigh (Oct-2006, 2011); depression; relapse of urinary tract infection
with resistant E. coli (ESBL) in Aug-2011; and penicillin allergy. Clinical findings showed reduced general state of health, could be woken, not fully oriented, slowed down, and personal anamnesis was not possible. Cor was reported to be
rhythmic and clean, and abdomen was noted to be soft, intestinal noises regular, no pressure pain. Liver and spleen palpatorily normal. Renal bed not painful on percussion. ECG showed sinus tachycardia, 118/min left location, regular times,
no specific final phase changes. X-ray thorax, AP lying down, was carried out on 28-Jun-2014, which revealed significantly twisted lying down x-rays, without certain evidence of infiltrate. Superior diaphragmatic coupola on both sides, in
the case of insufficient inspiration. No rough outgoing pleural effusions. Compared to the previous examination on 26-May-2014, decreasing congestion aspect, with known moderate chronic pulmonal venous congestion, aorta sclerosis,
omarthrosis right. On the same day of 28-Jun-2014, at 03:06 AM, laboratory tests included Quick INR of 28%, 2.5% (normal range: 80 to 130), PTT of 23.1 sec (normal range: 27 to 40), fibrinogen of 4.99 g/L (normal range: 1.5 to 4.5),
leucocytes of 17.2 Gpt/L (normal range: 4.3 to 10.0), erythrocytes of 3.4 Tpt/L (normal range: 4.1 to 5.4), haemoglobin of 91 g/L (normal range: 120 to 160), haematocrit of 0.30 unit not reported (0.36 to 0.48), and thrombocytes of 272 Gpt/L
(normal range: 166-387). On the same day of 29-Jun-2014, at 07:00 AM, laboratory tests included Quick INR of 4%, PTT of 26.5 sec, AT3 of 72.0% (normal range: 80 to 130), fibrinogen of 4.07 g/L, leucocytes of 15.6 Gpt/L, erythrocytes of
3.2 Tpt/L, haemoglobin of 83 g/L, haematocrit of 0.28 unit not reported, and thrombocytes of 226 Gpt/L. CT skull-CT skull native was carried out on 30-Jun-2014 which showed large subdural haematoma right hemisphere up to 2 cm seam
width. The subdural haemorrhages reach to the parafalxial. Compression of the right hemisphere parenchyma and midline relocation to contralateral up to 1.7 cm noted. Evidence of a haemorrhage in the parenchyma of the right basal ganglia
and significant compression of the right side ventricle noted. Compensatory, slightly expanded posterior horn of the left side ventricle noted. No decompensated cerebrospinal fluid accumulation, no incarceration, no petrosal bone cells were
noted and recorded paranasal sinuses were properly ventilated. Normal osseus skull structures noted. Sometimes pronounced motion artefacts win consecutive restricted assessability also noted. Overall assessment was reported as: large
subdural haematoma right, and basal ganglia bleeding right, midline relocation to the left, no incarceration and no cerebrospinal fluid accumulation. On the same day of 30-Jun-2014, at 05:00 AM, laboratory tests included leucocytes of 11.0
Gpt/L, erythrocytes of 3.2 Tpt/L, haemoglobin of 82 g/L, haematocirt of 0.26 unit nor reported, and thrombocytes of 16 Gpt/L. The patient was reported to the admitted to the observation ward. In the case of increased temperature and
infection constellation proven in the laboratory, and a radiologically suspected pulmonal infiltrate, antiobiosis was started. In the case of somnolence, the psychiatric medication was paused for the time being. With generous fluid substitution, it
was stated that the following day, it was possible for the patient to eat and take medication independently. Then, in the night from 30-Jun-2014 to 01-Jul-2014, there was a worsening in vigilance. The computer tomography of the skull, for
further diagnosis, then showed the aforementioned unfavourable finding (after consulting neurosurgery). The relatives were personally informed about the situation by the surgeon. A fall in our hospital can be ruled out, as the patient was in the
observation area at all times. A fall in the hospital was not described in the transfer letter, and in the CT findings from 27-Jun-2014, no haematoma or bleeding was described, meaning that ultimately a spontaneous incident whilst using
Falithrom must be assumed. It was reported that the patient was not admitted to a hospital because of the adverse reaction; the adverse reactions started during hospitalization. The events were also reported to be life threatening.
Treatment for these adverse events was not reported. On 01-Jul-2014, the investigator had an unscheduled visit to the patient. Outcome of the event lack of efficacy was not reported. On 01-Jul-2014, in the nighttime hours, the patient died

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

due to her pronounced cerebral damage. Causes of death were subdural hematoma right and basal ganglia hemorrhage right. It was not reported if an autopsy was performed. The reporter's opinion of causality between for the events of fatal subdural hematoma right and fatal basal ganglia hemorrhage right in relation to epoetin zeta was not related, while not reported in relation to lack of efficacy. Risk factors included thrombosis of deep vessels of lower extremities, hypertension, diabetes type 2 without vascular complications, cancer specified as ovarian cancer diagnosed on Jun-1996, and obesity with BMI of 32.0. It was also reported that the diabetes mellitus was from 18-May-2004 until 01-Jul-2014, and that the hypertension was from 02-Jun-2005 until 01-Jul-2014. 25-Nov-2013: Additional information was received from the same reporter regarding adverse event. 16-Jul-2014: Received additional information from the same reporter. Follow-up report was created to reflect additional information regarding patient details, medical history, suspect drug, adverse event and reporter's causality assessment. Recently died was added as adverse event; hence case was upgraded to serious. The patient's date of birth and race/ethnicity were updated. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure to other biosimilars. 28 Jul 2014: Corrected report was created to reflect this case as serious in the overall seriousness data field. 28-Jul-2014: Additional information was received from the same reporter. Follow-up information was received regarding adverse event and death details. The event death was updated to fatal subdural hematoma right and fatal basal ganglia bleeding right. 03-Sep-2014: Additional information was received from the same reporter. Follow-up report was created to reflect new information regarding adverse event and cause of death. 09-Dec-2014: Additional information was received from the same reporter. Reported term of event basal ganglia hemorrhage was updated to basal ganglia hemorrhage right. 09-Nov-2015: Additional information was received from the same reporter. Patient's day of birth was provided. Patient's height was also reported as 160 cm. The date when Retacrit treatment was changed to Aranesp was provided. Hyperlipidemia was added as medical history, while obesity was added as risk factor. Mean doses of the suspect drugs were also provided. It was also reported that the diabetes mellitus was from 18-May-2004 until 01-Jul-2014, and that the hypertension was from 02-Jun-2005 until 01-Jul-2014. It was reported that the patient did not experience any thromboembolic event during the treatment with other ESA, Aranesp. It was reported that the patient was not admitted to a hospital because of the adverse reaction; the adverse reactions started during hospitalization. The events were also reported to be life threatening. The reporter's opinion of causality for the events of fatal subdural hematoma right and fatal basal ganglia hemorrhage right was updated to not related. This information has been incorporated in the narrative and in the corresponding data fields. 19-Nov-2015: English translation of German text was received. Patient's history of allergy was provided. The patient's admission and hospitalization details were provided which included the reason for admission, treatment diagnoses, and other patient conditions. X-ray thorax and CT were added as diagnostic tests, while quick INR, PTT, fibrinogen, lucocytes, erythrocytes, haemoglobin, haematocrit, thrombocytes and AT3 were added as laboratory results. It was also reported that the patient died due to her pronounced cerebral damage. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Cannot provide causation without firm timeline, further objective clinical event details, medical history and concomitant medications. Follow-up: No change in previous assessment. Follow-up: New reported adverse event of death is probably not related to Retacrit given the multiple comorbidities in the medical history. Consider the death to be more likely due to progression of preexistent conditions, including the ovarian malignancy. Corrected report: No change in previous causality assessment. Follow-up: New reported adverse events subdural hematoma and basal ganglia bleeding are probably not related to Retacrit. Although the suspect drug can theoretically increase the risk of thrombosis, it seems unlikely for it to cause an acute cerebrovascular hemorrhage. Follow-up: No change in most recent causality assessment of probably not related. Follow-up: New information noted but does not warrant change in previous causality assessment. Follow-up: No change in previous company causality. Follow-up: No change in assessment, but company causality for both the hematoma and hemorrhage events are updated from probably not to not related based on the company's binary causality assessment guidelines.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	28-JUN-2014	Activated partial thromboplastin time	23.1 seconds	40 27
2	29-JUN-2014	Activated partial thromboplastin time	26.5 seconds	40 27
3	29-JUN-2014	Antithrombin III	72.0 %	130 80
4	26-MAY-2014	Chest X-ray	Not reported, Unknown	
5	28-JUN-2014	Chest X-ray	In the case of insufficient inspiration., Unknown	
6	28-JUN-2014	Chest X-ray	Certain evidence of infiltrate., Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	28-JUN-2014	Chest X-ray	No rough outgoing pleural effusions., Unknown	
8	28-JUN-2014	Chest X-ray	Congestion, aorta sclerosis,omarthrosis right., Un	
9	28-JUN-2014	Chest X-ray	Decreasing congestion aspect., Unknown	
10	28-JUN-2014	Chest X-ray	Significantly twisted lying down x-rays,without,	
11	28-JUN-2014	Chest X-ray	Superior diaphragmatic coupola on both sides, Un	
12	28-JUN-2014	Chest X-ray	With known moderate chronic pulmonal venous, Unk	
13	30-JUN-2014	Computerised tomogram head	Relocation to the left, no incarceration and no,	
14	30-JUN-2014	Computerised tomogram head	Right, and basal ganglia bleeding right, midline,	
15	30-JUN-2014	Computerised tomogram head	Overall assessment: large subdural haematoma, Unk	
16	30-JUN-2014	Computerised tomogram head	Cerebrospinal fluid accumulation, Unknown	
17		Electrocardiogram	Sinus tachycardia, 118/min left location, Unknown	
18		Electrocardiogram	Regular times, no specific final phase changes, U	
19	28-JUN-2014	Haematocrit	0.30, Unknown	0.48 0.36
20	29-JUN-2014	Haematocrit	0.28, Unknown	0.48 0.36
21	30-JUN-2014	Haematocrit	0.26, Unknown	0.48 0.36
22		Haemoglobin	10.0, Unknown	
23		Haemoglobin	12.3, Unknown	
24	22-MAY-2013	Haemoglobin	Too low, Unknown	
25	28-JUN-2014	Haemoglobin	91 g/l	160 120
26	29-JUN-2014	Haemoglobin	83 g/l	160 120
27	30-JUN-2014	Haemoglobin	82 g/l	160 120
28	28-JUN-2014	International normalised ratio	28, 2.5 %	130 80
29	29-JUN-2014	International normalised ratio	4 %	130 80
30	28-JUN-2014	Platelet count	272 Gpt/L, Unknown	387 166

Mfr. Control Number: 2021971

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
31	29-JUN-2014	Platelet count	226 Gpt/L, Unknown	387 166
32	30-JUN-2014	Platelet count	221 Gpt/L, Unknown	387 166
33	28-JUN-2014	Red blood cell count	3.4 Tpt/L, Unknown	5.4 4.1
34	29-JUN-2014	Red blood cell count	3.2 Tpt/L, Unknown	5.4 4.1
35	30-JUN-2014	Red blood cell count	3.2 Tpt/L, Unknown	5.4 4.1
36	28-JUN-2014	White blood cell count	17.2 Gpt/L, Unknown	10.0 4.3
37	29-JUN-2014	White blood cell count	15.6 Gpt/L, Unknown	10.0 4.3
38	30-JUN-2014	White blood cell count	11.0 Gpt/L, Unknown	10.0 4.3

13. Relevant Tests

CT-skull (30Jun2014): Overall assessment: large subdural haematoma, Unknown.
CT-skull (30Jun2014): Relocation to the left, no incarceration and no, Unknown.
CT-skull (30Jun2014): Right, and basal ganglia bleeding right, midline, Unknown.
ECG (Unknown Date): Regular times, no specific final phase changes, Unknown.
ECG (Unknown Date): Sinus tachycardia, 118/min left location, Unknown.
X-ray thorax (28Jun2014): Congestion, aorta sclerosis, omarthrosis right., Unknown.
X-ray thorax (28Jun2014): Significantly twisted lying down x-rays, without, Unknown.
X-ray thorax (28Jun2014): Superior diaphragmatic coupola on both sides, Unknown.
X-ray thorax (28Jun2014): With known moderate chronic pulmonal venous, Unknown.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption and tobacco usage were not reported. The patient had penicillin allergy. Medical history included hyperlipidemia from 05-Apr-2011 until 01-Jul-2014, chemotherapeutics-induced renal failure; and was diagnosed of renal failure on 01-Feb-1997. The patient was not on dialysis. The patient was not treated with an Erythropoiesis-Stimulating Agent (ESA) before the treatment with Retacrit, and she did not receive Retacrit prior the study. Risk factors included thrombosis of deep vessels of lower extremities, hypertension, diabetes type 2 without vascular complications, cancer specified as ovarian cancer diagnosed on Jun-1996, and obesity with BMI of 32.0. It was also reported that the diabetes mellitus was from 18-May-2004 until 01-Jul-2014, and that the hypertension was from 02-Jun-2005 until 01-Jul-2014. Race/Ethnicity: Caucasian. On 01-Jul-2014, in the nighttime hours, the patient died due to her pronounced cerebral damage. Causes of death were subdural hematoma right and basal ganglia hemorrhage right. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Depression (Depression);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism);
Unknown to Ongoing	Relevant Med History	Parathyroid adenoma (Parathyroid tumour benign);
Unknown to Ongoing	Relevant Med History	Dementia (Dementia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Pneumonia (Pneumonia);
Unknown to Ongoing	Relevant Med History	Recurrent urinary tract infection (Urinary tract infection);
Unknown to Ongoing	Relevant Med History	General physical health deterioration (General physical health deterioration);
Unknown	Relevant Med History	Adnexectomy (Salpingo-oophorectomy);
Unknown	Relevant Med History Mar 2004	Kidney transplant (Renal transplant);
Unknown	Relevant Med History	Hysterectomy (Hysterectomy);
Unknown	Relevant Med History Risk Factor	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor-BMI: 32.0	Obesity (Obesity);
Unknown	Relevant Med History Risk Factor-Diagnosed Jun-1996	Ovarian cancer (Ovarian cancer);
Unknown	Relevant Med History Risk Factor	Penicillin allergy (Drug hypersensitivity);
Unknown	Relevant Med History Risk Factor	Thrombosis of leg deep venous (Deep vein thrombosis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	14	AUG	1928	85 Years	Male	62.00 kg	20	NOV	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]
Stroke [Cerebrovascular accident]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 29-DEC-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2M329N2}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) Freq: 3 Week, Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 31-JAN-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CLOPIDOGREL (CLOPIDOGREL) ; Unknown
#2) PANTOPRAZOLE (PANTOPRAZOLE) ; Unknown
#3) RAMIPRIL (RAMIPRIL) ; Unknown
#4) TORASEMIDE (TORASEMIDE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Dialysis (Dialysis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2052813

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
13-FEB-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case describes a case of stroke.

This serious case from a physician (ref: 146-0003) describes an 85-year-old male patient who received Retacrit (epoetin zeta, three times a week, subcutaneous, batch number 2M329N2, dose not reported) for renal anaemia from 31-Jan-2011. Medical history and risk factor included hypertension. Past drug included Neorecormon (dose and route of administration not reported) for an unknown indication. Concomitant medications included ramipril (5 mg), torasemide (50 mg) both as arterial hypertension; clopidogrel (75 mg) for stenosis dialysis fistula and pantoprazole (20 mg) for dyspepsia; all given daily, routes of administration not reported.

On 31-Jan-2011, the patient started treatment with epoetin zeta. On 18-Nov-2013, the patient had haemoglobin of 7.4 mmol/l (normal range: 8.5-10.9 mmol/l). Last dose prior to the event was on 18-Nov-2013. On 20-Nov-2013, the patient had stroke, syncope and changes in personality leading to hospitalisation. On the same day of 20-Nov-2013, the patient had haemoglobin of 6.8 mmol/l, INR-1 of 1.20, aPTT of 33 s, and Quick test of 76 % (normal range: greater than 70%). On 21-Nov-2013, the patient had triglyceride of 0.69 mmol/l (less than 2.30), cholesterol of 3.89 mmol/l (less than 5.20), HDL-chol. of 2.58 (greater than 1.45), and LDL-chol. of 1.18 mmol/l (less than 3.90), On 23-Nov-2013, the patient had haemoglobin of 7.3 mmol/l, INR-1 of 1.14, aPTT of 33 s, and Quick test of 82%. Treatment for the event included neurological rehabilitation. Action taken with the suspect drug was not applicable. Outcome of the event was ongoing at the time of the report. However, it was also reported that the patient recovered on an unknown date.

The reporter's causality assessment between the event of stroke in relation to epoetin zeta was unlikely.

06-Dec-2013: Translation of the German texts was received. Follow-up report was created to reflect new information regarding the event, medical history and laboratory tests.

Pre-existing conditions included terminal renal failure, suspected MDS, s/p pacemaker implantation for AV block third degree. It was reported that on an unknown date, the patient had syncopation last night while in the bath, however the patient can remember nothing further. The patient returned to bed alone. His wife brought him to the RTS due to a change in character. On admission ward, there was multi-fragment olecranon fracture on the left today (on an unknown date) in dialysis since the patient normally undergoes dialysis 3x per week on site. Nurses and doctors in dialysis noticed a change in character in the patient and that the patient was not able to fix his gaze. Examination findings showed the patient was alert, adequately oriented with respect to all qualities, no headache, no meningism, nerve exit points free, cervical spine fully mobile, no aphasias/no dysarthria, no dizziness, no ringing in the ears and no tinnitus. On an unknown date, cerebral nerves examination showed pupils were isocoric, mw, LR direct/indirect prompt, hemianopsia towards the left/visual neglect on the left, no SPN, oculomotor preference to the right, incomplete gaze paresis to the left, via the median line, no DB, no facial paresis. Motor function examination on an unknown date showed no drop in arm extension test on the right and leg extension test on both sides, left olecranon fracture. Sensitivity examination appeared equal everywhere, no deficit indicating aesthesia or algesia. Reflexes showed moderately active and equal response on both sides to upper and lower stimulation, ASR non-stimulated on both sides, no clonus, no PBC. Coordination examination on an unknown date showed finger-nose test on the right metrical, not verifiable on the left, knee-heel-shin test possible on both sides. Stance/gait was not assessed. The patient was diagnosed with demarcation of the infarction in posterior flow area. The patient was admitted to STRU: KPL, radiographic kV diagnostics. The patient was scheduled for emergency surgery next week (unspecified) due to multi-fragment olecranon fracture on the left. However, the patient collapsed again in the ward, disoriented. Ischaemia, bleeding and RF excluded. On 20-Nov-2013, non-contrast cranial CT showed mid-sized interhemispherical gap. Extension of the inner and outer cerebrospinal fluid spaces, basal cisterns are delimitable. Extensive right occipital reduction in density below integration with the cortex, otherwise grey-white matter differentiation maintained. Symmetrical punctuate basal ganglia calcifications on both sides. No focal lesions of the thalami. Extensive white matter density reduction marked in the periventricular and subcortical regions. No new haemorrhage. There was limited ability to assess the posterior cranial fossa (beam hardening artefact). However, there was no evidence of extensive haemorrhage or density reduction. The patient had arteriosclerosis of the basal cerebral arteries. Paranasal sinuses and mastoid cells clear. No evidence of fracture in the bone windows. Diagnosis was compared with previous image from 07-Aug-2013, revealed demarcation of a posterior partial infarction on the right, likely subacute, no haemorrhage, changes to the white matter, likely microangiopathic basis and generalised loss of brain volume.

13-Feb-2014: Follow-up information was received from the same reporter. Follow-up report was created to reflect new information obtained regarding the suspect drug, adverse event, laboratory tests and medical history. Fatal acute myocardial infarction was added as an adverse event. Data entry correction was also made to reflect therapy start date of epoetin zeta as 31-Jan-2011.

Last dose of epoetin zeta prior to acute myocardial infarction was on 27-Dec-2013. On 29-Dec-2013, the patient had acute myocardial infarction described as chest pain. On the same day of 29-Dec-2013 at 13:52, CK was 7.46 mcmol/l (less than 3.20), CK-MB was 0.59 mcmol/l (less than 0.40), CK-MB% of CK 7.9% (less than 5%), myoglobin was 2741.0 mcg/l (less than 72) and troponin T was 230.7 pg/ml (less than 14). It was reported that the patient was not hospitalized and no treatment was given for the event. Action taken with the suspect drug was not reported.

On 29-Dec-2013, the patient died. Cause of death was acute myocardial infarction. It was not reported if an autopsy was performed.

The reporter's causality assessment for the event of acute myocardial infarction in relation to epotein zeta was unlikely.

Case Comment: Overall case causality: Probably Not Although the suspect drug can theoretically increase the risk of thrombosis by

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

increasing red blood cell concentration, this is unlikely in the current case as hemoglobin levels were still below normal at the time of the stroke. Patient also has significant cardiovascular risk factors. - N. Gonzales (04 Dec 2013)
Follow-up: No change in previous causality assessment. - N. Gonzales (18 Dec 2013)
Follow-up (18 Feb 2014): No change in
previous company assessment. - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	20-NOV-2013	Activated partial thromboplastin time	33 seconds	40 26
2	23-NOV-2013	Activated partial thromboplastin time	33 seconds	40 26
3	21-NOV-2013	Blood cholesterol	3.89 mmol/l	
4	29-DEC-2013	Blood creatine phosphokinase	7.46 umol/l	
5	29-DEC-2013	Blood creatine phosphokinase MB	0.59 umol/l	
6	29-DEC-2013	Blood creatine phosphokinase MB	7.9 %	
7	21-NOV-2013	Blood triglycerides	0.69 mmol/l	
8	20-NOV-2013	Computerised tomogram	No haemorrhage	
9	20-NOV-2013	Computerised tomogram	Likely, microangiopathic basis, Unknown	
10	20-NOV-2013	Computerised tomogram	Demarcation of a posterior partial infraction	
11	20-NOV-2013	Computerised tomogram	On the right likely subacute	
12	20-NOV-2013	Computerised tomogram	Generalised loss of brain volume	
13	20-NOV-2013	Computerised tomogram	Changes to the white matter	
14	18-NOV-2013	Haemoglobin	7.4 mmol/l	10.9 8.5
15	20-NOV-2013	Haemoglobin	6.8 mmol/l	10.9 8.5
16	23-NOV-2013	Haemoglobin	7.3 mmol/l	10.9 8.5
17	20-NOV-2013	High density lipoprotein	mmol/l	
18	21-NOV-2013	High density lipoprotein	2.58 mmol/l	
19	20-NOV-2013	International normalised ratio	1.20	1.25 0.90
20	23-NOV-2013	International normalised ratio	1.14	1.25 0.90
21	21-NOV-2013	Low density lipoprotein	1.18 mmol/l	
22	29-DEC-2013	Myoglobin blood	2741.0	
23		Neurological examination	Knee-heel-shin test	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			possible on both sides,Unknown	
24		Neurological examination	Finger-nose test on the right metrical, Unknown	
25		Neurological examination	Via the median line, Unknown	
26		Neurological examination	Pupils isocoric, mw, Unknown	
27		Neurological examination	No SPN, oculomotor preference to the right,Unknown	
28		Neurological examination	LR direct/indirect prompt, Unknown	
29		Neurological examination	Incomplete gaze paresis to the left, Unknown	
30		Neurological examination	Not assessed	
31		Neurological examination	No deficit indicating aesthesia or algesia	
32		Neurological examination	Moderately active	
33		Neurological examination	Appears equal everywhere	
34		Neurological examination	To upper and lower stimulation	
35		Neurological examination	Equal response on both sides	
36		Neurological examination	Visual neglect on the left, Unknown	
37		Neurological examination	Not verifiable on the left, Unknown	
38		Neurological examination	No drop in leg extension test on both sides,Unknow	
39		Neurological examination	ASR non-stimulated on both sides	
40		Neurological examination	No clonus, no PBC	
41		Neurological examination	Left olecranon fracture, Unknown	
42		Neurological examination	No drop in arm extension test on the right,Unknown	
43		Neurological examination	No DB, no facial paresis, Unknown	
44		Neurological examination	Hemianopsia towards the left, Unknown	
45		Physical examination	No aphasias/no dysarthria, Unknown	
46		Physical examination	Cervical spine fully mobile, Unknown	
47		Physical examination	No dizziness no ringing in ears no tinnitus,Unknow	
48	20-NOV-2013	Physical examination	Alert, adequately oriented with all qualities, Unk	

Mfr. Control Number: 2052813

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
49	20-NOV-2013	Physical examination	No headache no menigism nerve exit points free Unk	
50	20-NOV-2013	Prothrombin time	76 %	
51	23-NOV-2013	Prothrombin time	82 %	
52	29-DEC-2013	Troponin T	230.7	

13. Relevant Tests

Examination findings (20-Nov-2013): Alert, adequately oriented with all qualities
Examination findings (20-Nov-2013): No headache no menigism nerve exit points free
Non-contrast cranial CT compared with previous image from 07-Aug-2013 (20-Nov-2013): Demarcation of a posterior partial infraction
Myoglobin (29Dec2013): 2741.0 mcg/L
Troponin T (29Dec2013): 230.7 pg/mL

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption and tobacco usage were not reported. Medical history included hypertension. Past drug included Neocormon (dose and route of administration not reported) for an unknown indication Race/ Ethnicity: Caucasian 06-Dec-2013: Translation of the German text in the laboratory tests was received. Follow-up report was created to reflect additional information regarding medical history. Pre-existing conditions included terminal renal failure, suspected MDS, s/p pacemaker implantation for AV block third degree. 13-Feb-2014: Follow-up information was received from the same reporter. Follow-up report was created to reflect new information obtained regarding medical history. On 29-Dec-2013, the patient died. Cause of death was acute myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	MDS (Myelodysplastic syndrome);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Cardiac pacemaker insertion (Cardiac pacemaker insertion);
Unknown	Relevant Med History	Third degree AV block (Atrioventricular block complete);
22-JUN-2009 to 22-JUL-2011	Past Drug Event	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	08	MAR	1935	78 Years	Female	66.00 kg	02	SEP	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Stroke [Cerebrovascular accident]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously, for the treatment of renal anaemia. This report describes case of fatal stroke. This
serious case from a physician (ref: It-093-0005) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency and batch number not reported) for renal anaemia on an unknown date.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 02-SEP-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 91 IU/kg, (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 01-MAR-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2069922

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JUN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta. On an unknown date, the patient had stroke. Treatment for the event and action taken with epoetin zeta was not reported. On 02-Sep-2013, the patient died. Cause of death was stroke. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal stroke in relation to epoetin zeta was not reported.
The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered, batch number, date of expiry, previous exposure of patient to other biosimilars.
17-Jun-2014: Follow up information received from the same reporter. Follow up report created to reflect new information regarding patient details, medical history, suspect drug, and reporter's causality assessment. The patient's date of birth was updated. The patient was a female (height: 160 cm, dry weight: 66 kg). Medical history included diabetic nephropathy which led to renal failure diagnosed on 05-May-2010. It was reported the patient was not on dialysis and was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. The patient received Retacrit (total dosage/week of 91 IU/kg/week with frequency of 1 dosage/week) during week of entry into study from 01-Mar-2013.
The reporter's causality assessment for the event of fatal stroke in relation to Retacrit was updated to not related. Risk factors were reported as hypertension and diabetes type 2.

Case Comment: Overall case causality: Not assessable Cannot provide causation without firm timeline, objective clinical event details, pertinent laboratory work-up, medical history and concomitant medications. - N. Gonzales (10 Dec 2013) Follow-up (23 Jun 2014): New information noted. Overall and company causality changed to possible. Though patient has preexisting risk factors (hypertension and diabetes), cannot totally rule out possible contributory effect from the suspect drug.Retacrit can theoretically increase the risk of thromboembolic events by increasing red blood cell concentration and patient has been using the drug for six months. - N. Gonzales (23 Jun 2014)

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	91 IU/kg, Freq: 1 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	01-MAR-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage and medical history were not reported. On 02-Sep-2013, the patient died. Cause of death was stroke. It was not reported if an autopsy was performed. 17-Jun-2014: Follow up information received from the same reporter regarding medical history. Race/Ehtnicity: Caucasian. Medical history included diabetic nephropathy which led to renal failure diagnosed on 05-May-2010. It was reported the patient was not on dialysis and was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Risk factors were reported as hypertension and diabetes type 2.
Unknown to Ongoing	Relevant Med History 05-May-2010	Renal failure (Renal failure);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA		FEB	1933	80 Years	Male	70.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]
Heart rhythm disorder [Heart rate irregular]
Pulmonary thromboembolism [Pulmonary embolism]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that
it is an initial report.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 12-DEC-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) freuency 3

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 30-OCT-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FURANTHRIL [FUROSEMIDE] (FUROSEMIDE) ; Unknown
#2) TRITACE (RAMIPRIL) ; Unknown
#3) CARVEDILOL (CARVEDILOL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2004 to Unknown	Relevant Med History	Colon cancer (Colon cancer)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2085987

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-FEB-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Bulgaria, administered subcutaneously for the treatment of renal anaemia. This report describes a case of acute cardiac death, fatal heart rhythm disorder, fatal acute myocardial infarction, and fatal pulmonary thromboembolism. This serious case from a physician (reference: BG-014-0002) describes an 80-year-old male patient (weight: 70 kg and height: 175 cm) who received Retacrit from 30Oct2013 with frequency 3 subcutaneous for renal anaemia. The dose had not changed within 3 months prior the event. Past diseases of the patient reported as cancer: colon CA since 2004. There was no ischemic heart disease; hypertension and diarrhea. The patient had no history of hypersensitivities and drug dependence. Alcohol consumption and tobacco usage were not reported. Concomitant medications included carvedilol (6.25 mg/day), Furanthril (0.04 mg/day), and Tritace (5 mg/day); routes of administration not reported and given for unknown indications. On an unknown date, the patient started treatment with Retacrit. On an unknown date, the patient experienced acute cardiac death, heart rhythm disorder, pulmonary thromboembolism, and differential diagnosis of acute myocardial infarction. On 12-Dec-2013, the patient passed away suddenly while engaged in a coversation with the daughter. The most problem diagnosis has been specified in the death certificate as acute cardiac death, heart rhythm disorder, pulmonary thromboembolism, and differential diagnosis of acute myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment for the events of acute cardiac death, fatal heart rhythm disorder, fatal acute myocardial infarction, and fatal pulmonary thromboembolism in relation to Retacrit was not related. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered, batch number, date of expiry, and previous exposure of patient to other biosimilars. 28-Feb-2014: Additional information was obtained from the same reporter. Follow up report was created to delete the adverse event acute cardiac death. The reporter confirmed that the event acute cardiac death is the same with the event acute myocardial infarction. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number, date of expiry, and previous exposure of patient to other biosimilars. Additional information obtained in 08Feb2019 and 11Feb2019: Autopsy no performed. Type of dialysis reported as none (pre-dialysis). of death was confirmed as 12Dec2013 and cause of death reported as acute myocardial infarction.Hemoglobin was reported as 8 g/dl. The subject wasn't at any time exposed to any other erythropoietin stimulating against (ESA) and didn't experience any thromboembolic event during treatment with any other ESA. No risk factor for thromboembolic events was reported. The subject was not admitted in hospital and the event was not treated. No available laboratory/diagnostic results. The event not related to the suspect product as per investigator.

Follow-up (29Jan2019): This is a follow up report to notify that the case 2085987 and 08H-090-0315322-00 are duplicates. All subsequent follow-up information will be reported under manufacturer report number 2085987.

Follow-up (08Feb2019 & 11Feb2019) New reported information includes: subject information (date of birth, race), autopsy not performed, relevant medical history, suspect drug dosage information, lab data, event details (no treated, not admitted in hospital) and subject clinical courses.

Case Comment: Based on the information provided and drug's safety profile, the possible contribution of suspect drug epoetin zeta to the events fatal heart rhythm disorder, acute myocardial infarction and pulmonary thromboembolism cannot be excluded. More detailed information about medical history, concomitant drugs in this 80-year-old male patient would be helpful for further assessment. The impact of this report on the benefit/risk profile of the Pfizer product is evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators, as appropriate.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	8 g/dl	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	01	OCT	1938	75 Years	Male	56.00 kg	22	NOV	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Sweden, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal cardiac arrest.
This serious case from an investigator (ref: Sw-005-0014) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency, formulation, and batch number not reported) for renal anaemia

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 24-NOV-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 E,Freq: 1 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-SEP-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CALCIDON (ASCORBIC ACID, CALCIUM CARBONATE, ERGOCALC
#2) ETALPHA (ALFACALCIDOL) ; 27-APR-2011 / 23-NOV-2013
#3) WARAN (WARFARIN SODIUM) ; 06-AUG-2012 / 23-NOV-2013
#4) METOPROLOL (METOPROLOL) ; 06-NOV-2009 / 23-NOV-2013

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2188609

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
12-SEP-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

on an unknown date. Medical history included ischemic heart disease. Concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced cardiac arrest. Treatment for the adverse event and action taken with suspect drug were not reported. The patient died on 24-Nov-2013. Cause of death was cardiac arrest due to ischemic heart disease. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal cardiac arrest in relation to epoetin zeta was not related. 20-Mar-2014: Follow-up information received from the same reporter. Follow-up report created to reflect additional information regarding patient details, suspect drug, medical history, concomitant medications, laboratory tests, adverse event, and reporter's causality assessment. Life threatening was added as seriousness criterion. Adverse event fatal cardiac arrest was changed to fatal myocardial infarction. Patient was a 75-year-old male (weight: 56 kg and height: 182 cm). Patient's date of birth and ethnicity were reported. Patient was previously exposed to other erythropoietin-stimulating agent Mircera (234 mcg/kg/week). Additional medical history included hypertension. The patient had hemodialysis. Concomitant medications included metoprolol (200 mg, once a day), Waran (2.5 mg, by schedule), Calcidon (500 mg, twice a day), and Etalpha (0.75 mcg, once every second day); routes of administration not reported, all given for unknown indications. Dose and frequency of suspect drug Retacrit were 4000 E and once a week, respectively (batch number was unknown). Date of first dose was 01-Sep-2011 while date of last dose prior to the adverse event was 19-Nov-2013. It was reported that on 21-Nov-2013, the patient was hospitalized due to dyspnea. On the same day of 21-Nov-2013 at 17:15, laboratory tests revealed troponin T hs 149 ng/L (ref: <15), hemoglobin 136 g/L (ref: 134-170), EVF 0.44 (0.40-0.50), erythrocytes 4.1 x10^12/L (ref: 4.3-5.7), MCV 106 fL (ref: 82-98), MCH 33 pg (ref: 27-33), MCHC 311 g/L (ref: 320-360), thrombocytes 197 x10^9/L (ref: 140-350), leukocytes 11.9 x10^9/L (ref: 3.5-8.8), PK-INR 1.9 (ref: 0.8-1.2), CRP 26 mg/L (ref: <10), and NT-proBNP >35,000 ng/L (ref: <1800). On 22-Nov-2013, the patient was diagnosed with myocardial infarction due to ischemic heart disease. Treatment of the adverse event included palliative treatment. Cause of death was changed to myocardial infarction due to ischemic heart disease. The reporter's causality assessment for the event of fatal myocardial infarction in relation to epoetin zeta was unlikely. 12-Sep-2014: Follow-up information received from the same reporter. Follow-up report was created to reflect additional information regarding medical history. It was reported that the patient had previously experienced myocardial infarction during treatment with past drug Mircera from 05-Apr-2011 until 15-Apr-2011. Risk factor included smoking.

Case Comment: Overall case causality: Not related The event is due to the patient's underlying ischemic heart condition. - R. Jacot (11 Feb 2014) Follow-up (25 Mar 2014): Overall case causality: Probably not Hospira causality: Not related No change in previous company assessment. - R. Jacot Follow-up: No change in previous assessment. - N. Gonzales (21 Sep 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	21-NOV-2013	C-reactive protein	26 mg/l	
2	21-NOV-2013	Haematocrit	0.44, Unknown	0.50 0.40
3	21-NOV-2013	Haemoglobin	136 g/l	170 134
4	21-NOV-2013	International normalised ratio	1.9, Unknown	1.2 0.8
5	21-NOV-2013	Mean cell haemoglobin	33 pg	33 27
6	21-NOV-2013	Mean cell haemoglobin concentration	311 g/l	360 320
7	21-NOV-2013	Mean cell volume	106, FL	98 82
8	21-NOV-2013	N-terminal prohormone brain natriuretic peptide	Greater than 35,000, NG/L	
9	21-NOV-2013	Platelet count	197 x10 9/l	350 140
10	21-NOV-2013	Red blood cell count	4.1 x10 12/l	5.7 4.3
11	21-NOV-2013	Troponin T	149, NG/L	
12	21-NOV-2013	White blood cell count	11.9 x10 9/l	8.8

Mfr. Control Number: 2188609

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				3.5

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) CALCIDON (ASCORBIC ACID, CALCIUM CARBONATE, ERGOCALCIFEROL, PYRIDOXINE HYDROCHLORIDE) ;
26-JAN-2011 / 23-NOV-2013

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Medical history included ischemic heart disease. Allergies, alcohol consumption and tobacco usage were not reported. The patient died on 24-Nov-2013. Cause of death was cardiac arrest due to ischemic heart disease. It was not reported if an autopsy was performed. 20-Mar-2014: Follow-up information received from the same reporter. Follow-up report created to reflect additional information regarding medical history. Patient was previously exposed to other erythropoietin-stimulating agent Mircera (234 ng/kg/week). Additional medical history included hypertension. The patient had hemodialysis. Cause of death was changed to myocardial infarction due to ischemic heart disease. Race/Ethnicity: Caucasian. 12-Sep-2014: Follow-up information received from the same reporter. Follow-up report was created to reflect additional information regarding medical history. It was reported that the patient experienced myocardial infarction during treatment with past drug Mircera from 05-Apr-2011 until 15-Apr-2011. Risk factor included smoking.
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown to Ongoing	Relevant Med History Risk Factor	Smoker (Tobacco user);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
22-JUN-2010 to 29-AUG-2011	Past Drug Event	MIRCERA (MIRCERA); Drug Indication: Drug therapy (Drug therapy), Drug Reaction: Myocardial infarction (Myocardial infarction)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
PRIVACY	GERMANY			1948	65 Years	Female	61.70 kg	06	DEC	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal myocardial infarction. This serious case from a physician (ref: Ge-463-0015) describes a 65-year-old female patient (weight: 61.7 kg; height: 153 cm) who received Retacrit (epoetin zeta; subcutaneous, once a week; batch number 2I298I2; dose not reported) for renal anaemia since 26-Aug-2013.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 06-DEC-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2I298I2}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 22-AUG-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL HEXAL (ALLOPURINOL) ; Unknown
#2) BICANORM (SODIUM BICARBONATE) ; Unknown
#3) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX) ; Unknown
#4) GABAPENTIN 1A PHARMA (GABAPENTIN) ; Unknown
#5) HUMINSULIN NORMAL (INSULIN HUMAN) ; Unknown
#6) MOXONIDIN 1 A PHARM (MOXONIDINE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension)
Unknown to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2233652

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-MAY-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included hyperlipidemia, diabetes mellitus, and hypertension. It was reported that the patient was not, at any time, exposed to any other erythropoetin-stimulating agent (ESA). Allergies, alcohol consumption, and tobacco usage were not reported. Concomitant medications included metoprolol succinat Al 47.5 (2-0-1-0-0, piece, oral, daily), torasemid ABZ 10 mg tablet (1-0-0-0-0; route of administration not reported), allopurinol Hexal 100 (0-0-1-0-0; route of administration not reported), Bicanorm (2-2-2-0-0, piece, oral, daily), pantoprazol Hexal 40 mg (1-0-0-0-0, piece, oral, daily), Huminsulin Normal (10-4-8-0-0, IE, subcutaneous, daily), Ferrlecit 40 mg (2-0-0-0-0, ampules, intravenous, weekly), Vocado 40 mg/10 mg (1-0-0-0-0, piece, oral, daily), Monoxidin 1A Pharma 0.3 mg (1-0-1-0-0, piece, oral, daily), Tevacidol 0.5 mcg soft capsules (alfacalcidol; 1-0-0-0-0, piece, oral, daily), gabapentin 1A Pharma 100 mg (0-0-1-0-0, piece, oral, daily), renagel 800 mg (0-1-1-0-0, piece, oral, daily), and illegible drug entry (dose and route of administration not reported); all for unknown indications. On 26-Aug-2013, the patient started treatment with epoetin zeta. On 06-Dec-2013, the patient experienced myocardial infarction and was hospitalized on the same day. Troponin I on the same day at 00:57 was at 0.012 ng/ml (normal value: less than 0.028). Treatment for the adverse event and action taken with epoetin zeta were not reported. The patient died on 06-Dec-2013. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal myocardial infarction in relation to epoetin zeta was not related. Risk factors included Cimino shunt surgery on Jul-2013 and artherosclerotic heart disease. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered.
14-Apr-2014: Follow up report was received from the same reporter. Follow up report was created to reflect additional information regarding the suspect drug, medical history, and diagnostic examinations. The reporter was able to provide the following information for the identification and traceability of the biosimilar product epoetin zeta: dosage administered. Dosage of Retacrit was 8000 IE. Medical history of hypertension was also reported as arterial hypertension, atherosclerotic heart disease was also reported as atherosclerotic coronary disease, and diabetes mellitus was further described as non-primary insulin-dependent or type 2 diabetes. Additional medical history included paroxysmal atrial fibrillation with oral anticoagulation with Falithrom and chronic kidney disease stage 5 with dialysis scheduled on Dec-2013. The patient was assigned to emergency treatment. The patient conveyed to the emergency physician that at around 23:30 on an unknown date, she tried to call her son but was no longer able to speak. Her son then went to check on her, discovered her barely conscious, and noted that she could not move her left arm anymore. On admission, the patient was suffering from psychomotor restlessness, was vomiting, and exhibited hemiparesis of the left side. General clinical findings on admission showed good overall health, good physical condition and nutritional status. Tonsillar ring somewhat covered by vomit. Teeth in poor state. No goitre. Cardiovascular examination showed pure heart tones, arrhythmic heart action but normal frequency. Pulmonary examination showed vesicular breath sounds with no crepitations. Abdomen showed soft abdominal walls, adipose, no pain on palpitation or rebound tenderness, no resistances, borborygmus audible, liver and spleen palpable, and no renal angle tenderness. The patient had tattoo on the right upper arm. Pulseless upper right extremity, pallid and cold. Neurological findings showed no meningism. No pain on percussion of the cranial vault or neural exit points. Pupils average dilation, symmetrical reaction to light. No gaze paresis. Also other cranial nerves intact as far as can be ascertained. No speech changes. Proprioceptive reflexes of the left upper extremities diminished, lower extremities on both sides normal activity. Babinski reflex positive on left. No abdominal reflex. Slack hemiparesis on the left. Sensitivity and coordination could not be assessed. No tremor. The patient had cold sweat, no fever. Psychological findings showed that the patient was somnolent to soporific, exhibited psychomotor restlessness, and therefore no further examination possible. ECG showed intermediate heart axis, sinus rhythm 75/min. In view of the clinical progression, suspected anoxic T-wave via the front wall. EEG on 06-Dec-2013 showed moderate changes of a general nature. No lesion. No evidence of elevated cerebral susceptibility to seizures. CT - non-contrast cranial showed age-appropriate image of the subarachnoid spaces and cerebral parenchyma, no evidence of infarction, no haemorrhage or space-occupying lesion. Infratentorial overlap from image artefact resulting in limited ability to assess. The imaging diagnostics (cCT non-contrast) showed no evidence for new infarct demarcation or haemorrhage. The morning after admission, the neurological deficit was significantly regressed (NIH 20 to NIH 2 pt.), so that differential diagnosis led to consider that a possible complex focal seizure had occurred with Todd's paresis. The patient then had an EEG performed and during this exam, cardiac arrest took place suddenly and the patient required resuscitation. Unfortunately the resuscitation was unsuccessful and the patient died on 06- Dec-2013.
As per 26Mar2020 it was reported that there was no dialysis ("pre-dialyis") reported. Retacrit was given at 4000 IU weekly from 22Aug2013 (Hemoglobin measured on 15Aug2013- 7,9 g/dl) and at 8000 IU weekly from 25Sep2013 (hemoglobin measured on 17Sep2013- 7,6 g/dl). Hemoglobin after the dosage switch (measured on 05Dec2013)- 9,0 g/dl. No other erythropoietin-stimulating factors were given to the patient. Previously reported in medical history Diabetes mellitus was specified as type 2 Diabetes mellitus, Artherosclerotic heart disease was ongoing (comment: "state after AM (acute myocarditis) in June 2019"), Paroxysmal atrial fibrillation occured on 26Nov2013 (comment- "Falithrom"). Medical history additionally included transient ischemic attack in 2013, ongoing renal insufficiency stage 5 (comment- "shunt insertion done"). Relevant data from provided hospital records: "hospitalized from 06Dec2013 to 06Dec2013 in neurological department. Diagnoses:1. exitus lethalis in acute myocardial infarction; 2. Atherosclerotic heart disease, 3. arterial hypertension; 4. non-primary insulin-dependent diabetes mellitus [type-2 diabetes]; 5. paroxysmal atrial fibrillation, oral anticoagulation with falithrom; 6. chronic kidney disease, stage 5, planned dialysis Dec2013; 7. Hyperlipidemia. The patient was admitted to the emergency room. As per ambulance physician she tried to call her son around 11:30, but couldn't say anything. He then looked for her, found her unconscious, and noticed that she cannot move her left arm anymore. During admission-psychomotorical unrest, vomiting and hemiparesis left. Cardiac sounds pure, cardiac actions arrhytmic, but normofrequent. Upper right extremity with no pulse, pale, cold. Babinski sign left positive. Cold sweat, no fever. Patient is somnolent to soporous. ECG: indifferent type, sinus rhythm, 75/min, taking clinical course into account, suspicion of suffocation-T over the anterioir wall. Therapy and course: in cCT naive no signs of a fresh infarct demarcation or bleeding. In the morning after admission neurological deficit was remarkably regredient (NIH 20 to NIH 2 points), so we thought about possible complex-focal attack with Todd s paresis. Thereupon the patient received EEG and during this examination an asystole occurred suddenly and the patient required resuscitation. Unfortunately it was unsuccessful and the patient died on 06Dec2013. Relevant (out of scope) lab data provided: 15Aug2013: RBC- 2.8x1012/l (normal range- 3.9- 5.3), hematocrit: 0.25 l/l (normal range- 0.36-0.47), hemoglobin- 7.9 g/dl (normal

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

range- 12-16), urea- 29.6 mmol/l (normal range-1.7-8.3), creatinine- 469 umol/l (ULN- 80), GFR- 8 ml/min-1 (normal range- 54-114), uric acid- 428 umol/l (normal range- 137-363); 17Sep2013: MCHC- 29.8 mmol/l (normal range- 30-36), RBC- 2.9x1012/l, hematocrit: 0.26 l/l, hemoglobin- 7.6 g/dl, MCH- 26.5 pg (normal range- 28-32), phosphorus anorganic- 1.97 mmol/l (normal range- 0.8-1.6), parathormone- 118 mg/l (normal range- 16-65), urea- 28.8, creatinine- 458, GFR- 8, uric acid- 428; 16Oct2013: RBC- 3.4, hematocrit- 0.28, hemoglobin- 8.6, MCH- 25.4, phosphorus anorganic- 2.71, urea- 23.6, creatinine- 478, GFR- 8; 05Dec2013: leukocytes- 9.9x109/l (normal range- 4-9), hematocrit- 0.29, hemoglobin- 9, MCH- 27.1, potassium- 5.4 mmol/l (normal range- 3.5-5.1), phosphorus anorganic- 2.2, parathormone- 133, urea- 32.5, creatinine- 575, GFR- 6, uric acid- 387.

Follow-up (04Mar2019): New information received from the investigator includes updated patient's age. (patient is 65 years old).

Follow-up (08Mar2019): New information received from the investigator includes confirmation of patient's age.

Follow-up (26Mar2020): New information received from investigator includes: clinical course; lab data.

Follow-up (19May2020): New information received from investigator includes: confirmation that patient received Retacrit weekly.

Case Comment: Overall case causality: Not related Noting reporter's assessment, the event is more likely due to the patient's underlying atherosclerotic heart disease with contributory effects from other reported cardiac risk factors. - (17 Mar 2014) Follow-up (28 Apr 2014): No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	15-AUG-2013	Blood creatinine	469 umol/l	80
2	17-SEP-2013	Blood creatinine	458 umol/l	80
3	16-OCT-2013	Blood creatinine	478 umol/l	80
4	05-DEC-2013	Blood creatinine	575 umol/l	80
5	17-SEP-2013	Blood parathyroid hormone	118 mg/l	65 16
6	05-DEC-2013	Blood parathyroid hormone	133 mg/l	65 16
7	17-SEP-2013	Blood phosphorus	1.97 mmol/L	1.6 0.8
8	16-OCT-2013	Blood phosphorus	2.71 mmol/L	1.6 0.8
9	05-DEC-2013	Blood phosphorus	2.2 mmol/L	1.6 0.8
10	05-DEC-2013	Blood potassium	5.4 mmol/L	5.1 3.5
11	15-AUG-2013	Blood urea	29.6 mmol/L	8.3 1.7
12	17-SEP-2013	Blood urea	28.8 mmol/L	8.3 1.7
13	16-OCT-2013	Blood urea	23.6 mmol/L	8.3 1.7
14	05-DEC-2013	Blood urea	32.5 mmol/L	8.3 1.7
15	15-AUG-2013	Blood uric acid	428 umol/l	363 137
16	17-SEP-2013	Blood uric acid	428 umol/l	363 137
17	05-DEC-2013	Blood uric acid	387 umol/l	363 137
18		Breath sounds	vesicular breath sounds	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			with no crepitations	
19		Cardiovascular evaluation	Pulseless upper right extremity, pallid, cold	
20		Cardiovascular evaluation	arrhythmic heart action but normal frequency	
21		Computerised tomogram head	no haemorrhage or space-occupying lesion	
22		Computerised tomogram head	and cerebral parenchyma,no evidence of infarction	
23		Computerised tomogram head	no evidence for new infarct demarcation	
24		Computerised tomogram head	or haemorrhage	
25		Computerised tomogram head	age-appropriate image of subarachnoid spaces	
26		Electrocardiogram	suspected anoxic T-wave via the front wall	
27		Electrocardiogram	intermediate heart axis	
28	06-DEC-2013	Electrocardiogram	moderate changes of a general nature	
29	06-DEC-2013	Electrocardiogram	cerebral susceptibility to seizures	
30	06-DEC-2013	Electrocardiogram	No lesion. No evidence of elevated	
31		Gastrointestinal examination	soft abdominal walls, adipose	
32		Gastrointestinal examination	no resistances, borborygmus audible	
33		Gastrointestinal examination	no renal angle tenderness	
34		Gastrointestinal examination	no pain on palpitation or rebound tenderness	
35		Gastrointestinal examination	liver and spleen palpable	
36	15-AUG-2013	Glomerular filtration rate	8 ml/min	114 54
37	17-SEP-2013	Glomerular filtration rate	8 ml/min	114 54
38	16-OCT-2013	Glomerular filtration rate	8 ml/min	114 54
39	05-DEC-2013	Glomerular filtration rate	6 ml/min	114 54
40	15-AUG-2013	Haematocrit	0.25 l/l	0.47 0.36
41	17-SEP-2013	Haematocrit	0.26	0.47 0.36
42	16-OCT-2013	Haematocrit	0.28	0.47 0.36
43	05-DEC-2013	Haematocrit	0.29	0.47 0.36
44	15-AUG-2013	Haemoglobin	7.9 g/dl	16

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				12
45	17-SEP-2013	Haemoglobin	7.6 g/dl	16 12
46	25-SEP-2013	Haemoglobin	7.6 g/dl	16 12
47	16-OCT-2013	Haemoglobin	8.6 g/dl	16 12
48	05-DEC-2013	Haemoglobin	9.0 g/dl	16 12
49		Heart sounds	Pure heart sounds	
50	17-SEP-2013	Mean cell haemoglobin	26.5 pg	32 28
51	16-OCT-2013	Mean cell haemoglobin	25.4 pg	32 28
52	05-DEC-2013	Mean cell haemoglobin	27.1 pg	32 28
53	17-SEP-2013	Mean cell haemoglobin concentration	29.8 mmol/L	36 30
54		Neurological examination	neurological deficit significantly regressed	
55		Neurological examination	NIH 20 to NIH 2 pt	
56		Neurological examination	No abdominal reflex	
57		Neurological examination	No gaze paresis. Other cranial nerves intact	
58		Neurological examination	No pain on percussion of the	
59		Neurological examination	No speech changes	
60		Neurological examination	No tremor. Had cold sweat. No fever	
61		Neurological examination	Proprioceptive reflexes of the left	
62		Neurological examination	Pupils average dilation	
63		Neurological examination	Sensitivity, coordination could not be assessed	
64		Neurological examination	showed no meningism	
65		Neurological examination	Slack hemiparesis on the left	
66		Neurological examination	upper extremities diminished	
67		Neurological examination	symmetrical reaction to light	
68		Neurological examination	Babinski reflex positive on left	
69		Neurological examination	cranial vault or neural exit points	
70		Neurological examination	lower extremities both	

Mfr. Control Number: 2233652

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			sides normal activity	
71		Physical examination	good physical condition and nutritional status	
72		Physical examination	Tonsillar ring somewhat covered by vomit	
73		Physical examination	Teeth in poor state. No goitre.	
74		Physical examination	good overall health	
75		Psychiatric evaluation	somnolent to soporific	
76		Psychiatric evaluation	exhibited psychomotor restlessness	
77	15-AUG-2013	Red blood cell count	2.8 x10 12/l	5.3 3.9
78	17-SEP-2013	Red blood cell count	2.9 x10 12/l	5.3 3.9
79	16-OCT-2013	Red blood cell count	3.4 x10 12/l	5.3 3.9
80		Sinus rhythm	75/min	
81	06-DEC-2013	Troponin I	0.012 ng/ml	0.028
82	05-DEC-2013	White blood cell count	9.9 x10 9/l	9 4

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	8000 IU, weekly; Unknown	Renal anaemia (Nephrogenic anaemia)	25-SEP-2013 / 29-NOV-2013; 66 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) PANTOPRAZOL HEXAL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Unknown

#8) RENAGEL /01459901/ (SEVELAMER) ; Unknown

#9) TORASEMID ABZ (TORASEMIDE) Tablet ; Unknown

#10) VOCADO (AMLODIPINE BESILATE, OLMESARTAN MEDOXOMIL) ; Unknown

#11) ALFACALCIDOL (ALFACALCIDOL) ; Unknown

#12) METOPROLOL SUCCINATE (METOPROLOL SUCCINATE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Dialysis (Dialysis);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
26-NOV-2013 to Unknown	Relevant Med History Falithrom	Paroxysmal atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Atherosclerotic cardiovascular disease (Arteriosclerosis); state after acute myocarditis in June 2019
Unknown	Relevant Med History Jul-2013	Cimino shunt (Arteriovenous fistula operation);
Unknown	Past Drug Event	FALITHROM (FALITHROM); Drug Indication: Anticoagulant therapy (Anticoagulant therapy)
2013 to Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown to Ongoing	Relevant Med History	Renal insufficiency (Renal failure);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	09	JUN	1929	84 Years	Male	65.00 kg	24	APR	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischemic brain stroke [Ischaemic stroke]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal ischemic
brain stroke. This serious case from an investigator (reference: Bg-014-0004) describes an 84-year-old male patient (weight: 65 kg and height: 180 cm) who received Rectacrit (epoetin zeta; 3 x 3000 E/weekly, dose was also reported as

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 24-APR-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3x 3000 E/weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anaemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 04-NOV-2013 / 21-JUL-2014

19. THERAPY DURATION
#1) 260 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) MADOPAR (BENSERAZIDE HYDROCHLORIDE, LEVODOPA) ; 01-JAN-2003 / 23-APR-2014

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Since 2003 until Apr-2014	Parkinson's disease (Parkinson's disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2327613

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
29-APR-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2327613

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

138 IU/kg/week, 3 times a week; subcutaneous, formulation and batch number not reported) for anaemia from 04-Nov-2013 to 21-Apr-2014. Medical history included Parkinson's disease since 2003 until Apr-2014 and glumerulonephritis leading to renal failure diagnosed in Dec-2012. It was reported that the patient was not exposed to any other erythropoetin-stimulating agent. Concomitant medications included Madopar (125 mg, 3 times a day, route of administration not reported) for Parkinson's disease. On 04-Nov-2013, the patient began treatment with epoetin zeta. On 21-Apr-2014, the patient received the last dose of the suspect drug. On 24-Apr-2014, the patient developed ischemic brain stroke. Treatment for the adverse event was reported as not applicable. On 24-Apr-2014, the patient died. Cause of death was ischemic brain stroke. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal ischemic brain stroke in relation to epoetin zeta was not assessable. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number and date of expiry.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without further objective clinical event details, including laboratory test results and post-mortem findings. - R. Jacot (02 May 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included Parkinson's disease since 2003 until Apr-2014 and glumerulonephritis leading to renal failure diagnosed in Dec-2012. It was reported that the patient was not exposed to any other erythropoetin-stimulating agent. On 24-Apr-2014, the patient died. Cause of death was ischemic brain stroke. It was not reported if an autopsy was performed. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History Dec-2012	Renal failure (Renal failure);
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	11	OCT	1925	88 Years	Female	60.00 kg	11	MAY	2014	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Middle left cerebral artery infarction [Cerebral infarction]
Respiratory insufficiency due to leftside brain ischemia [Cerebral ischaemia]
Respiratory insufficiency due to leftside brain ischemia [Respiratory failure]

Case Description: Fatal middle left cerebral artery infarction, fatal respiratory insufficiency due to leftside brain ischemia. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (reference: Ge-093-0085), which

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 12-MAY-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3X019Z3}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 196.7 IU/k (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 08-JAN-2014 / 19-JUN-2007

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ZOPICLON (ZOPICLONE) ; 22-NOV-2013 / 01-MAY-2014
#2) FUROSEMID /00032601/ (FUROSEMIDE) ; 22-NOV-2013 / 01-MAY-2014
#3) ISMN (ISOSORBIDE MONONITRATE) ; 22-NOV-2013 / 01-MAY-2014
#4) MOLSIDOMIN (MOLSIDOMINE) ; 22-NOV-2013 / 01-MAY-2014
#5) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 2
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Gastritis erosive (Gastritis erosive)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2400091

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-JAN-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

refers to an 88-year-old Caucasian female patient (height: 164 cm, dry weight: 60.0 kg). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history included chronic erosive gastritis and hypertensive nephropathy leading to renal failure first diagnosed on 21-Nov-2013. The patient was on hemodialysis from 22-Nov-2013 (average of 3 dialysis per week). The patient was not treated with an ESA before treatment with Retacrit. Concomitant medications included molsidomin (4 mg), ISMN (20 mg), both given daily as prophylaxis; pantoprazol (40 mg, daily) for acid regurgitation, Zopiclon (7.5 mg, daily) for sleeping disorders, and furosemide (250 mg) for oliguria; all routes of administration were not reported. The patient began treatment with Retacrit (epoetin zeta, 196.7 IU/Kg/week, 3 dosage per week, subcutaneous; batch number 3X019Z3) for renal anaemia from 08-Jan-2014. On 07-Apr-2014, investigations revealed hematocrit 25.1% (standard reference range: F: 37-47), erythrocytes 3.34 x10^6/mcl (3.9-5), leukocytes 5.9 x10^3/mcl (4.3-10), thrombocytes 155 x10^3/mcl (150-400), cholesterol 176 mg/dl (0-200), HDL cholesterol 58 mg/dl (35-100), triglycerides 56 mg/dl (0-200), and LDL cholesterol (direct) 111 mg/dl (up to 155). Most recent laboratory values taken on an unknown date showed: hematocrit 26.3, erythrocytes 3.5 x10^6/mcl, leukocytes 5.1 x10^3/mcl, thrombocytes 243 x10^3/mcl, cholesterol 152 mg/dl, HDL cholesterol 51 mg/dl, triglycerides 76 mg/dl, and LDL cholesterol (direct) 96 mg/dl. The patient received last dose of epoetin zeta prior to the event on 09-May-2014. On 11-May-2014, the patient was admitted to the stroke unit due to a left-sidecerebral infarction suspected on the basis of a severe brachiofacial hemiparesis arising during the admission process. The CCT (cranial computer tomography) was performed immediately on the same day indicated no evidence of a new ischaemic heart event, bleeding or space-occupying lesion; the only item of note was a previous partial posterior infarction of the middle right cerebral artery approximately 5cm with distinct hypodense cortical to subcortical demarcation; Patchy non-homogenous hypodense microangiopathic changes to the frontal white matter on both sides. It was reported that there was limited ability to examine brain stem and cranial fossa due to movement artefacts; as far as could be seen, normal. During her inpatient stay, the patient exhibited deteriorating vigilance. On the same day of 11-May-2014, the patient experienced respiratory insufficiency due to leftside brain ischemia. On 12-May-2014, the patient was in a deep coma. The patient had become increasingly unstable in terms of respiration and haemodynamics. After consulting with the patient's daughter, transfer to the intensive care ward and, if necessary, cardiopulmonary resuscitation, was declined. Oral medication was terminated due to the reduced vigilance. Insertion of a stomach probe was also declined. Action taken with the suspect drug was not reported. On 12-May-2014 at 10:30, the patient died. Causes of death were middle left cerebral artery infarction and respiratory insufficiency due to leftside brain ischemia. It was not reported if an autopsy was performed. The reporter's causality assessment between the events of fatal middle left cerebral artery infarction and fatal respiratory insufficiency due to leftside brain ischemia and epoetin zeta was reported as not assessable. Risk factors included coronary heart disease (ischemic heart disease) which occurred in Jan-2004, atrial fibrillation, pulmonary embolism, hypertension, heart failure NYHA stage IV, and peripheral arterial disease. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 27-JAN-2015: Additional information was received from the same reporter. Adverse event was changed from death to fatal middle left cerebral artery infarction and fatal respiratory insufficiency due to leftside brain ischemia. Life threatening and hospitalisation were added as seriousness criteria. Additional information was also received regarding update of patient's date of birth to 11-Oct-1925 and weight to 60 kg; addition of chronic erosive gastritis as medical history and update of dialysis to hemodialysis; concomitant medications; lot number and date of last dose of epoetin zeta prior to the event; further clinical event details, laboratory and diagnostic tests data, change of date of death from 14-May-2014 to 12-May-2014; and addition of peripheral arterial disease as risk factor. It was reported that risk factor coronary heart disease (ischemic heart disease) occurred in Jan-2004. These information have been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible (reporter causality not reported) Hospira causality: Probably Not Noting a diagnosis of hypertensive nephropathy and the presence of significant comorbidities as risk factors (coronary heart disease, atrial fibrillation, heart failure and pulmonary embolism), consider patient's death to be more likely due to progression of preexistent conditions. Cannot provide a more definitive assessment without autopsy findings and further objective details. - N. Gonzales (16 Jun 2014) Follow-up: Overall case causality: Not assessable (reporter causality is not assessable) Hospira causality: Not related New information noted. The updated adverse events are unlikely to be due to the suspect drug. Even if Retacrit can theoretically increase the risk of thromboembolic events, patient has significant comorbidities and cardiovascular risk factors which far outweigh the potential risk from the suspect drug. These include coronary heart disease since 2004, atrial fibrillation, pulmonary embolism, hypertension, heart failure and peripheral arterial disease. - N. Gonzales (05 Feb 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood cholesterol	152 mg/dl	200 0
2	07-APR-2014	Blood cholesterol	176 mg/dl	200 0
3		Blood triglycerides	76 mg/dl	200

Mfr. Control Number: 2400091

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				0
4	07-APR-2014	Blood triglycerides	56 mg/dl	200 0
5	11-MAY-2014	Computerised tomogram head	to subcortical demarcation, Unknown	
6	11-MAY-2014	Computerised tomogram head	and cranial fossa due to movement artefacts, Unkno	
7	11-MAY-2014	Computerised tomogram head	with distinct hypodense cortical, Unknown	
8	11-MAY-2014	Computerised tomogram head	Patchy non-homogenous hypodense, Unknown	
9	11-MAY-2014	Computerised tomogram head	No evidence of a new ischaemic heartevent, Unknown	
10	11-MAY-2014	Computerised tomogram head	microangiopathic changes, Unknown	
11	11-MAY-2014	Computerised tomogram head	Limited ability to examine brain stem, Unknown	
12	11-MAY-2014	Computerised tomogram head	bleeding or space-occupying lesion, Unknown	
13	11-MAY-2014	Computerised tomogram head	Middle right cerebral artery approximately 5cm, Un	
14	11-MAY-2014	Computerised tomogram head	Previous posterior infarction of the, Unknown	
15	11-MAY-2014	Computerised tomogram head	To the frontal white matter on both sides, Unknown	
16	11-MAY-2014	Computerised tomogram head	As far as could be seen, normal., Unknown	
17		Haematocrit	26.3 %	47 37
18	07-APR-2014	Haematocrit	25.1 %	47 37
19		High density lipoprotein	51 mg/dl	100 35
20	07-APR-2014	High density lipoprotein	58 mg/dl	100 35
21		Low density lipoprotein	96 mg/dl	
22	07-APR-2014	Low density lipoprotein	111 mg/dl	
23		Platelet count	243, X10**3/MCL	400 150
24	07-APR-2014	Platelet count	155, X10**3/MCL	400 150
25		Red blood cell count	3.5, X10**6/MCL	5 3.9
26	07-APR-2014	Red blood cell count	3.34, X10**6/MCL	5 3.9
27		White blood cell count	5.1, X10**3/MCL	10 4.3

Mfr. Control Number: 2400091

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
28	07-APR-2014	White blood cell count	5.9, X10**3/MCL	10 4.3

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3X019Z3}; Regimen #1	196.7 IU/kg/week, Freq: 3 week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	08-JAN-2014 / 19-JUN-2007; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#5) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 22-NOV-2013 / 01-MAY-2014

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included chronic erosive gastritis and hypertensive nephropathy leading to renal failure first diagnosed on 21-Nov-2013. The patient was on hemodialysis from 22-Nov-2013 (average of 3 dialysis per week). The patient was not treated with an ESA before treatment with Retacrit. Risk factors included coronary heart disease (ischemic heart disease) which occurred in Jan-2004, atrial fibrillation, pulmonary embolism, hypertension, heart failure NYHA stage IV, and peripheral arterial disease. On 12-May-2014 at 10:30, the patient died. Causes of death were middle left cerebral artery infarction and respiratory insufficiency due to leftside brain ischemia. It was not reported if an autopsy was performed. Race/ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History 21-Nov-2013	Renal failure (Renal failure);
Unknown	Relevant Med History	Cerebral infarct (Cerebral infarction);
Unknown	Relevant Med History Risk Factor	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History Risk Factor: Ischemic heart disease	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor	Heart failure NYHA class IV (Cardiac failure chronic);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History Risk Factor	Pulmonary embolism (Pulmonary embolism);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	22-Nov-2013, ave 3 per week	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	29	NOV	1937	76 Years	Male	65.00 kg	25	MAY	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischemic brain stroke [Ischaemic stroke]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Bulgaria, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal gastritis
errosiva. This serious case from an investigator (reference: Bg-004-0004) describes a male patient (height: 170 cm, dry weight: 65 kg; age not reported) who received Retacrit (epoetin zeta, 94 IU/kg/week, 3 dosage/week, subcutaneous;

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 25-MAY-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2H289I2; Exp.Dt. 01-NOV-2014}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 94 IU/kg/ (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 27-MAY-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic pyelonephritis (Pyelonephritis chronic)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2400201

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-JUN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2400201

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

batch number not reported) for renal anaemia from 27-May-2013. Medical history included chronic pyelonephritis which led to renal failure diagnosed on 01-May-2013. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the study. The patient was not treated with an ESA before treatment with Retacrit. Concomitant medications were not reported. On 27-May-2013, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced gastritis errosiva. Treatment for the adverse event and action taken with the suspect drug were not reported. The patient died on 25-May-2014. Cause of death was gastritis errosiva. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal gastritis errosiva in relation to epoetin zeta was not reported. Risk factors included coronary heart disease, atrial fibrillation, cerebrovascular disease, hypertension and heart failure NYHA stage III. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure of patient to other biosimilars. 11-Jul-2014: Additional information was received from the investigator. Follow-up report created to reflect new information regarding adverse event, suspect drug, medical history and laboratory test. The reporter was able to provide the following information regarding the identification and traceability of Retacrit: batch number, date of expiry and previous exposure of patient to other biosimilars. The adverse event was updated to fatal ischemic brain stroke. Batch number of Retacrit was 2H289I2. The patient had no previous exposure to other biosimilars. On 25-May-2014, the patient experienced ischemic brain stroke. On unknown dates, laboratory tests included Hb at 76 g/l and Hct at 0.34 (normal value not reported). Treatment for the adverse event included mannitol 10% (250 ml, intravenous), fraxiparine (2 x 0.6 unit and route of administration not reported) and Trifas (2 x 10 mg, intravenous). According to the investigator, there was no relationship between the event and treatment with Retacrit. The patient had mitral valve prosthesis since 2008, atrial fibrillation and heart failure 3-4 degree before admission. The patient also had two ischemic brain strokes before starting Epo treatment.

Case Comment: Overall case causality: Possible (reporter causality not reported) Hospira causality: Not assessable Cannot provide causation of event without further objective clinical event details and concomitant medications. Based on the nature of the event, it is important to get a detailed gastrointestinal history and list of oral medications to aid in providing a causality assessment. - N. Gonzales (17 Jun 2014) Follow-up: Overall case and company causality: Possible New information noted. Updated adverse event of ischemic brain stroke is possibly related. Though the patient has significant cardiovascular risk factors (mitral valve prosthesis, atrial fibriallation and previous stroke), cannot totally rule out possible contributory effects from the suspect drug. Retacrit can theoretically increase the risk of thromboembolic events based on mechanism of action. - N. Gonzales (20 Jul 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	0.34, Unknown	
2		Haemoglobin	76 g/l	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2H289I2; Exp.Dt. 01-NOV-2014}; Regimen #1	94 IU/kg/ week, Freq:3 Week, Interval:1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	27-MAY-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption and tobacco usage were not reported. Medical history included chronic pyelonephritis which led to renal failure diagnosed on 01-May-2013. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the study. The patient was not treated with an ESA before treatment with Retacrit. Risk factors included coronary heart disease, atrial fibrillation, cerebrovascular disease, hypertension and heart failure NYHA stage III. The patient died on 25-May-2014. Cause of death was gastritis errosiva. It was not reported if an autopsy was performed. Race/Ethnicity: Caucasian. 11-Jul-2014: Additional information was received from the investigator. Follow-up report created to reflect new information regarding medical history. The patient had no previous exposure to other biosimilars. Cause of death was updated to ischemic brain stroke.

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		The patient had mitral valve prosthesis since 2008, atrial fibrillation and heart failure 3-4 degree before admission. The patient also had two ischemic brain strokes before starting Epo treatment.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Ischemic stroke (Ischaemic stroke);
Unknown	Relevant Med History Since 2008	Cardiac valve prosthesis user (Cardiac valve prosthesis user);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Unspecified cerebrovascular disease (Cerebrovascular disorder);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	10	APR	1942	71 Years	Female	76.00 kg	01	NOV	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lower leg thrombosis [Thrombosis]
Stroke [Cerebrovascular accident]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report from Germany describes a case of
fatal stroke and lower leg thrombosis.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 22-MAY-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 25 IU/kg/w (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 07-DEC-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2400258

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-JUN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2400258

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case from an investigator (reference: Ge-083-0008) describes a 71-year-old female patient (height: 174 cm; dry weight: 76 kg) who received Retacrit (epoetin zeta, 25 IU/kg/week, once per week, subcutaneous, batch number unknown) for renal anaemia from 07-Dec-2011. Medical history included coronary heart disease, hypertension leading to renal failure diagnosed in 2010, atrial fibrillation, non-small cell lung cancer diagnosed in 2010, former stroke and former myocardial infarction. The patient was not treated with an ESA before treatment with Retacrit. The patient was not on dialysis. The patient's BMI was 25.1. Concomitant medications were not reported. On 07-Dec-2011, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced stroke. On an unknown day in Nov-2013, the patient experienced lower leg thrombosis. Treatment for the adverse events and action taken with epoetin zeta were not reported. Outcome of lower leg thrombosis was unknown at the time of the report. On 22-May-2014, the patient died. Cause of death was stroke. It was not reported if an autopsy was performed. The reporter's causality assessment for the events of fatal stroke and lower leg thrombosis in relation to epoetin zeta was not related. Risk factors included arterial hypertension, myocardial infarction, and non-small cell lung cancer diagnosed in 2010. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 24-Aug-2015: Corrected report has been created to change patient's age to 71-year-old (previously reported as 72-year-old), year of birth to 1942 (previously reported as 1962) and height to 174 cm (previously reported as 176 cm) in the narrative and corresponding data field.

Case Comment: Overall case causality: Not related Events are not related as patient had preexistent cardiovascular risk factors and comorbidities even prior to drug administration. Investigator also considered the events not related to Epoetin. Corrected report: No change in previous causality assessment.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	25 IU/kg/week, Freq: 1 week, Interval:1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	07-DEC-2011 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included coronary heart disease, hypertension leading to renal failure diagnosed in 2010, atrial fibrillation, non-small cell lung cancer diagnosed in 2010, former stroke and former myocardial infarction. The patient was not treated with an ESA before treatment with Retacrit. The patient was not on dialysis. Risk factors included arterial hypertension, myocardial infarction, and small cell lung cancer diagniosed in 2010. Race/ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History 2010	Renal failure (Renal failure);
Unknown	Relevant Med History	Hypertension arterial (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History 2010	Non-small cell lung cancer (Non-small cell lung cancer);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GREECE	01	JAN	1932	81 Years	Male	80.00 kg	21	AUG	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Greece, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal myocardial
infarction. This serious case from an investigator (ref: Gr-031-0004) describes a male patient (weight: 80 kg and height: 180 cm; age not reported) who received Retacrit (epoetin zeta; 75 IU/kg/week, one dosage per week, subcutaneous,

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 21-AUG-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 75 IU/kg, Freq: 1 Day, Interval:10	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anaemia of chronic renal failure (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 26-MAR-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATORVASTATIN (ATORVASTATIN) ; 03-AUG-2010 / 21-AUG-2013
#2) DIAMICRON (GLICLAZIDE) ; 03-AUG-2010 / 21-AUG-2013
#3) GALVUS (VILDAGLIPTIN) ; 21-JUN-2011 / 21-AUG-2013
#4) LASIX /00032601/ (FUROSEMIDE) ; 09-AUG-2010 / 21-AUG-2013
#5) SALOSPIR (ACETYLSALICYLIC ACID) ; 03-AUG-2010 / 21-AUG-2013

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2411460

24c. DATE RECEIVED BY MANUFACTURER
21-JUL-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

(Continued on Additional Information Page)

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

batch number not reported) for renal anaemia from 26-Mar-2013. Medical history included diabetic nephropathy which led to renal failure diagnosed on 09-Aug-2010. The patient was not treated with an ESA before treatment with Retacrit and did not receive Retacrit prior to study. Concomitant medications were not reported. On 26-Mar-2013, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced myocardial infarction. Treatment for the adverse event and action taken with suspect drug were not reported. The patient died on 20-Aug-2013. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal myocardial infarction in relation to epoetin zeta was not reported. Risk factors included cerebrovascular disease, stroke, type 2 diabetes with diabetic vascular complications. Patient was an ex-smoker. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure of patient to other biosimilars. 21-Jul-2014: Follow-up report received from the same reporter. Follow-up report created to reflect additional information regarding patient details, suspect drug, medical history, concomitant medications, adverse event, and reporter's causality assessment. Hospitalisation and life threatening were added as seriousness criteria. Patient's age was 81 years with BMI of 24.7. Indication of suspect drug Retacrit was updated to anaemia of chronic renal failure and frequency was changed to once every 10 days. It was reported that the patient was not exposed to any other erythropoetin-stimulating agent. Other medical history included hypertension known from 2000. Concomitant medications included Lasix (40 mg, twice daily) for renal failure, Salospir (100 mg, once daily) for cerebrovascular disease, Galvus (50 mg, once) for diabetes mellitus, Diamicron (30 mg, once) for diabetes mellitus, and Atrost (atorvastatin; 20 mg once/day) for hyperlipidemia; routes of administration not reported. The patient received last dose of epoetin zeta prior to the adverse event on 15-Aug-2013. Event onset date was 21-Aug-2013. It was reported that the patient was hospitalised in the intensive care unit on 21-Aug-2013. Date of death was changed to 21-Aug-2013. The reporter's causality assessment for the event of fatal myocardial infarction in relation to epoetin zeta was unlikely. Risk factor stroke occurred in 2006 while diabetes mellitus was known from 2000. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Possible Although patient has significant cardiovascular risk factors for infarction, cannot totally rule out possible contributory effects from the suspect drug. Retacrit can theoretically increase the risk of thromboembolic events by increasing red blood cell concentration. - N. Gonzales (24 Jun 2014) Follow-up: New information noted but does not warrant change in previous causality assessment. Case remains possibly related. - N. Gonzales (30 Jul 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Medical history included diabetic nephropathy which led to renal failure diagnosed on 09-Aug-2010. The patient was not treated with an ESA before treatment with Retacrit and did not receive Retacrit prior to study. Allergies and alcohol consumption were not reported. Race/Ethnicity: Caucasian. Risk factors included cerebrovascular disease, stroke, type 2 diabetes with diabetic vascular complications. Patient was an ex-smoker. The patient died on 20-Aug-2013. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. 21-Jul-2014: Follow-up report received from the same reporter. Follow-up report created to reflect additional information regarding medical history. It was reported that the patient was not exposed to any other erythropoetin-stimulating agent. Other medical history included hypertension known from 2000. Date of death was changed to 21-Aug-2013. Risk factor stroke occurred in 2006 while diabetes mellitus was known from 2000.
Unknown to Ongoing	Relevant Med History 2000	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History 09-Aug-2010	Renal failure (Renal failure);
Unknown	Relevant Med History	Cerebrovascular disorder (Cerebrovascular disorder);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);

Mfr. Control Number: 2411460

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History 2006	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History 2000	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

25b. Name And Address of Reporters continued
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	05	APR	1942	71 Years	Male	74.00 kg	18	MAR	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart attack [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Greece, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal heart attack.
This serious case from an investigator (reference: Gr-003-0012) describes a 71-year-old male patient (height: 167 cm and weight: 74 kg; age not reported) who received Retacrit (epoetin zeta, 10000 IU, once a week, subcutaneous, batch

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 18-MAR-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, Freq: 1 week, Interval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-DEC-2012 / 18-MAR-2014

19. THERAPY DURATION
#1) 473 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DILATREND (CARVEDILOL) ; Unknown
#2) MIXTARD /00806401/ (INSULIN HUMAN, INSULIN HUMAN INJECT
#3) MONOSORDIL (ISOSORBIDE MONONITRATE) ; Unknown
#4) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown
#5) RENVELA (SEVELAMER CARBONATE) ; Unknown
#6) SALOSPIR (ACETYLSALICYLIC ACID) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2453067

24c. DATE RECEIVED BY MANUFACTURER
31-JUL-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

(Continued on Additional Information Page)

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

number unknown) for renal anemia from 01-Dec-2012 to 18-Mar-2014. The patient had no known drug hypersensitivities and drug dependence, and was not at any time exposed to any other erythropoetin-stimulating agent (ESA). Medical history included diabetes mellitus type 2 and hypertension since 1999; hyperlipidemia, ischemic heart disease, and peripheral arterial disease since an unknown date; and diabetic nephropathy which led to renal failure diagnosed on an unknown day in Jan-2011. It was reported that the patient was not on dialysis. Concomitant medications included Plavix (75, once a day), Salospir (100, once a day), Monosordil 20 (20, three times a day), and Dilatrend (6.25, twice a day) for ischemic heart disease; Renvela (850, three times a day) for hyperphosphatemia, and Mixtard (30/70, three times a day) for diabetes mellitus; all units of doses and routes of administration not reported. On 01-Dec-2012, the patient started treatment with epoetin zeta (dose also reported as 135.13 IU/kg/week). Informed consent was signed on 26-May-2013. However, it was also reported that the patient did not receive Retacrit prior to the study. On an unspecified date, the reporter stated that the patient received Retacrit (10000 IU/week) and there was no reaction. On an unknown day in Mar-2014, the patient received the last dose of epoetin zeta prior to the event. On 18-Mar-2014, the patient experienced heart attack. Treatment for the adverse event and action taken with the suspect drug were reported as not applicable. Therapy end date of epoetin zeta was also reported as on 18-Mar-2014. The patient died suddenly at home on 18-Mar-2014. Cause of death was heart attack. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal heart attack in relation to the study medication epoetin zeta was not related. The reporter stated that the heart attack was due to ischemic heart disease. Risk factors included diabetic vascular complications, vascular anomalies (unspecified), coronary heart disease, cerobrovascular disease, transient cerebral ischemic attack, and the patient was an ex-smoker. Concurrent conditions of peripheral arterial disease, hyperlipidaemia, hypertension, and diabetes mellitus type 2 were identified as risk factors. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 31-Jul-2014: Follow-up information was obtained from the same reporter. Follow-up report was created to reflect additional information regarding medical history. The reporter was able to provide information regarding the previous exposure of the patient to other biosimilars. The patient did not have previous exposure to other biosimilars. No autopsy was performed.

Case Comment: Overall case causality: Possible Though patient has significant cardiovascular risk factors in the medical history, consider also possible contributory effects from the suspect drug. Retacrit can theoretically increase the risk of thromboembolic events based on known drug mechanism of action. - N. Gonzales (22 Jul 2014) Follow-up: No change in previous causality assessment. - N. Gonzales (08 Aug 2014)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) MIXTARD /00806401/ (INSULIN HUMAN, INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption was not reported. The patient had no known drug hypersensitivities and drug dependence, and was not at any time exposed to any other erythropoetin-stimulating agent (ESA). Medical history included diabetes mellitus type 2 and hypertension since 1999; hyperlipidemia, ischemic heart disease, and peripheral arterial disease since an unknown date; and diabetic nephropathy which led to renal failure diagnosed on an unknown day in Jan-2011. It was reported that the patient was not on dialysis. Risk factors included diabetic vascular complications, vascular anomalies (unspecified), coronary heart disease, cerobrovascular disease, transient cerebral ischemic attack, and the patient was an ex-smoker. Concurrent conditions of peripheral arterial disease, hyperlipidaemia, hypertension, and diabetes mellitus type 2 were identified as risk factors. The patient died suddenly at home on 18-Mar-2014. Cause of death was heart attack. It was not reported if an autopsy was performed. Race/Ethnicity: Caucasian. 31-Jul-2014: Follow-up information was obtained from the same reporter. The patient did not have previous exposure to other biosimilars. No autopsy was performed.
Unknown to Ongoing	Relevant Med History Jan-2011	Renal failure (Renal failure);
Unknown	Relevant Med History	No adverse reaction (No adverse event);

Mfr. Control Number: 2453067

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Unspecified cerebrovascular disease (Cerebrovascular disorder);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History 1999	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History 1999	Hypertension (Hypertension);
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Transient cerebral ischemia (Transient ischaemic attack);
Unknown	Relevant Med History	Vascular anomaly (Vascular malformation);

25b. Name And Address of Reporters continued
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	BULGARIA	25	MAY	1945	69 Years	Male	65.00 kg	25	JUN	2014	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart attack [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Bulgaria, administered subcutaneously for the treatment of renal anaemia. This report describes a case of fatal heart attack.
This serious case from an investigator (reference: Bg-001-0024) describes a male patient (age not reported; height: 178 cm, dry weight: 65 kg) who received Retacrit (epoetin zeta; subcutaneous) (dose and frequency not reported; batch

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 25-JUN-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 24-JAN-2014 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	 Relevant Med History	() Pyelonephritis (Pyelonephritis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2574411

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-OCT-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

number unknown) for renal anaemia from 24-Jan-2014. The patient had not been exposed and had not experienced any thromboembolic event to any erythropoetin-stimulating agent (ESA). Medical history included pyelonephritis which led to renal failure diagnosed on an unknown date. It was reported that the patient was not on dialysis. Concomitant medications were not reported. On 24-Jan-2014, the patient started treatment with epoetin zeta. Date of enrollment was on 06-Feb-2014. Current treatment of Retacrit during week of entry was also received on 06-Feb-2014 with dose at 89 IU/kg/week, 2 dosage/week. On an unknown date, the patient experienced heart attack. Treatment for the adverse event and action taken with the suspect drug were not reported. The patient died on 25-Jun-2014. Cause of death was heart attack. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal heart attack in relation to epoetin zeta was possible. Risk factors included hyperlipidaemia and history of smoking. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered and previous exposure of patient to other biosimilars

Case Comment: Overall case causality: Possible Retacrit can theoretically increase the risk of thromboembolic events by increasing red blood cell concentration, but cannot provide a more defintive assessment without firm timeline of drug administration, pertinent laboratory findings and other cardiovascular risk factors, if any. - N. Gonzales (11 Oct 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. The patient had not been exposed and had not experienced any thromboembolic event to any erythropoetin-stimulating agent (ESA). Medical history included pyelonephritis which led to renal failure diagnosed on an unknown date. It was reported that the patient was not on dialysis. The patient died on 25-Jun-2014. Cause of death was heart attack. It was not reported if an autopsy was performed. Risk factors included hyperlipidaemia and history of smoking. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	10	SEP	1926	86 Years	Female	57.00 kg	30	AUG	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction. Epoetin zeta. Serious Hospira sponsored clinical study report (reference: Gr-051-0005) from Greece, received from a physician, which refers to an 86-year-old female Caucasian patient (weight: 57 kg; height:
159 cm, also reported as 157 cm). Patient's medical history included cardiorenal syndrome (CRS) which led to renal failure diagnosed in 2009. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 30-AUG-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 149.25 IU/ (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 17-MAY-2013 / 30-AUG-2013

19. THERAPY DURATION
#1) 106 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) EXFORGE (AMLODIPINE BESILATE, VALSARTAN) ; Unknown
#2) IBUTIN (TRIMEBUTINE MALEATE) ; Unknown
#3) LIPITOR (ATORVASTATIN CALCIUM) ; Unknown
#4) ZANTAC (RANITIDINE HYDROCHLORIDE) ; Unknown
#5) ZYLAPOUR (ALLOPURINOL) ; Unknown
#6) OTHER THERAPEUTIC PRODUCTS ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Cardiorenal syndrome (Cardiorenal syndrome)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2602755

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-OCT-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2602755

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

study. The patient was not pregnant nor lactating. The patient had no known drug hypersensitivities and no history of drug dependence. The patient was not treated with an ESA before treatment with Retacrit. Concomitant medications included Lipitor 20 for dyspilidemia, Ibutin 300 for irritable bowel, Zantac 150 for stomach protection, Zylapour 300 for coronary heart disease; Exforge 60 and an illegible drug, both for CHD and hypertension. Doses and routes for all concomitant medications were 1x1 and oral, respectively. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. On 17-May-2013, the patient started treatment with Retacrit (epoetin zeta, 149.25 IU/kg/week, 2 dosage/week, dose also reported as 10000/week, subcutaneous; batch number unknown) for renal anaemia. Date informed consent was signed was on 24-May-2013. On 30-Aug-2013, the patient was admitted in a hospital due to myocardial infarction. On an unknown date, haemoglobin was 10.0 and haematocrit was 34.3 (units of measurement and normal values not reported). Treatment for the adverse event and action taken with the suspect drug in response to the adverse event were not reported. However, therapy end date of epoetin zeta was reported to be on 30-Aug-2013. On 30-Aug-2013, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event of fatal myocardial and the suspect drug epoetin zeta was not related. Risk factors included coronary heart disease, hyperlipidaemia, hypertension, and heart failure NYHA stage III. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Probably Not Although the suspect drug can theoretically increase the risk of thromboembolic events by mechanism of action, the patient has been on Retacrit for just a few months. The multiple cardiovascular risk factors in the medical history (coronary heart disease, hyperlipidaemia, hypertension, and heart failure) outweigh the potential risk from the suspect drug. - N. Gonzales (30 Oct 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	34.3, Unknown	
2		Haemoglobin	10.0, Unknown	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	149.25 IU/kg, Freq: 2 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	17-MAY-2013 / 30-AUG-2013; 106 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption and tobacco usage were not reported. Patient's medical history included cardiorenal syndrome (CRS) which led to renal failure diagnosed in 2009. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the study. The patient was not pregnant nor lactating. The patient had no known drug hypersensitivities and no history of drug dependence. The patient was not treated with an ESA before treatment with Retacrit. On 30-Aug-2013, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. Risk factors included coronary heart disease, hyperlipidaemia, hypertension, and heart failure NYHA stage III. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Irritable bowel (Irritable bowel syndrome);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);

Mfr. Control Number: 2602755

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	04	MAR	1932	81 Years	Female	60.00 kg	20	OCT	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiac arrest [Cardiac arrest]
Myocardial infarction [Myocardial infarction]

Case Description: Fatal cardiac arrest and fatal myocardial infarction. Epoetin zeta. Serious Hospira sponsored clinical study report from Greece received from a health professional (reference: Gr-051-0031), which refers to a 81-year-old female Caucasian
patient (height: 160 cm, dry weight: 60 kg).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 29-OCT-2013
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IU, 1 (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 03-SEP-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DIOVAN (VALSARTAN) ; Unknown
#2) LASIX /00032601/ (FUROSEMIDE) ; Unknown
#3) NORVASC (AMLODIPINE BESILATE) ; Unknown
#4) ZYLORIC (ALLOPURINOL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2605484

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-OCT-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2605484

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient's medical history included peripheral arterial disease, and hypertensive nephropathy which led to renal failure diagnosed on 10-Feb-2010. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit, and did not receive Retacrit prior the study. Concomitant medications included Diovan 160 (1x1, oral), Norvasc 5 (1x1, oral), and Lasix 60 (1x1 every 3 weeks, oral), all for hypertension; and Zyloric 100 (1x1, oral) for hyperuricemia. On 03-Sep-2013, the patient started treatment with Retacrit (epoetin zeta; 6000 IU per week, dose also reported as 100 IU/kg/week; 1 dosage per week, subcutaneous, solution for injection in pre-filled syringe; batch number unknown) for renal anemia. The patient signed the consent and was included in the study on 14-Oct-2013. On 20-Oct-2013, the patient experienced myocardial infarction and cardiac arrest. On the same day, the patient was admitted. Action taken with epoetin zeta was not reported. On the same day of 29-Oct-2013, the patient died. The patient did not complete the study because of her death. It was reported that the patient died due to cardiac arrest and myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal cardiac arrest and fatal myocardiac infarction in relation to epoetin zeta was not related. Risk factors included hypertension and breast cancer diagnosed in 2005. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Probably Not Although the suspect drug can theoretically increase the risk of thromboembolic events based on known drug mechanism of action, this is highly unlikely as patient was started on Retacrit only a week before. Patient also has major significant risk factors which outweigh any potential risk from the drug. - N. Gonzales (31 Oct 2014)

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	6000 IU, 100 IU/kg/week, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	03-SEP-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. Patient's medical history included, peripheral arterial disease, and hypertensive nephropathy which led to renal failure diagnosed on 10-Feb-2010. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit, and did not receive Retacrit prior the study. Risk factors included hypertension and breast cancer diagnosed in 2005. Race/Ethnicity: Caucasian On 29-Oct-2013, the patient died. The patient did not complete the study because of her death. It was reported that the patient died due to cardiac arrest and myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History Diagnosed 10 Feb 2010	Renal failure (Renal failure);
Unknown	Relevant Med History Risk Factor- 2005	Breast cancer (Breast cancer);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	29	AUG	1943	Unk	Male	67.50 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]

Case Description: Acute myocardial infarction. Epoetin zeta. Serious Hospira sponsored study report from Italy received from an investigator (ref: It-116-0021) which refers to a Caucasian male patient (age not reported) (weight: 67.5 kg also reported as dry
weight: 75 kg; height: 175 cm). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously for the treatment of renal

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 13-NOV-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anemia in CKD (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPINE (AMLODIPINE) ; Unknown
#2) ATORVASTATIN (ATORVASTATIN) ; Unknown
#3) FUROSEMIDE (FUROSEMIDE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Cardiomyopathy (Cardiomyopathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2649763

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-NOV-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2649763

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

anaemia. The patient had no history of drug dependence. Medical history included allergy to Rocefin, cardiopathy, and glomerulonephritis which led to renal failure diagnosed in 29-Nov-2012. The patient had been on dialysis, thrice weekly, since 25-Nov-2013. The patient was not treated with an erythropoiesis-stimulating agent before treatment with Retacrit. Concomitant medications included amlodipine (10 mg, 1 c x 2 day), atorvastatin (20 mg, 1 c/day) and furosemide (500 mg 1/2 c x 2/week) (routes of adminsitration not reported); all given for unknown indications. On 16-Oct-2013, prior to the study, the patient started treatment with Retacrit (epoetin zeta, 4000 UI/week , subcutaneous; lot number unknown) for anemia in CKD. However, it was reported that the patient's first ever Retacrit treatment was on 24-Oct-2014. It was reported that on 27-Nov-2013, the patient was enrolled to the study and signed the informed consent. During the week of entry into the study, the patient received Retacrit (57 IU/kg/week, 1 dosage per week). On 13-Nov-2014, the patient experienced acute myocardial infarction. Treatment for the adverse event was not reported. It was reported that after the reported adverse experience, dosage of the suspect drug continued unchanged. On 13-Nov-2014, the patient died. Cause of death was acute myocardial infarction. It was not reported if an autopsy was performed. The reporter’s opinion of causality for the event fatal acute myocardial infarction in relation to epoetin zeta was not related. Risk factors included cerebrovascular disease, hypertension, heart failure NYHA stage IV and being an ex-smoker. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): previous exposure of patient to other biosimilars.

Case Comment: .Overall case causality: Probably Not Although the suspect drug can theroetically increase the risk of thrombosis and infarction by increasing red cell concentration, patient had numerous cardiovascular risk factors which far outweigh the potential risk from the suspect drug. - N. Gonzales (02 Dec 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption was not reported. The patient had no history of drug dependence. Medical history included allergy to Rocefin, cardiopathy, and glomerulonephritis which led to renal failure diagnosed in 29-Nov-2012. The patient had been on dialysis, thrice weekly, since 25-Nov-2013. The patient was not treated with an erythropoiesis-stimulating agent before treatment with Retacrit. Risk factors included cerebrovascular disease, hypertension, heart failure NYHA stage IV, and being an ex-smoker. Race/ Ethnicity: Caucasian On 13-Nov-2014, the patient died. Cause of death was acute myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Allergic reaction to antibiotics (Drug hypersensitivity);
Unknown	Relevant Med History	Cerebrovascular disorder (Cerebrovascular disorder);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Heart failure NYHA class IV (Cardiac failure chronic);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Dialysis (Dialysis);
Unknown	Past Drug Event	ROCEFIN (ROCEFIN); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	14	JUL	1928	86 Years	Male	77.00 kg	19	NOV	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

A. cerebri posterior infarction [Cerebral infarction]
Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction and A.cerebri posterior infarction. Epoetin zeta. Hospira sponsored study report received from an investigator (ref: Ge-152-0025) which refers to a patient. The patient was enrolled in a Hospira-Sponsored
Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 09-OCT-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3T002V3; Exp.Dt. 01-DEC-2015}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 U, So (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 27-JAN-2014 / 20-NOV-2014

19. THERAPY DURATION
#1) 298 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) OSTEOTRIOL (CALCITRIOL) ; 10-MAY-2012 / Unknown
#2) TORASEMID (TORASEMIDE) ; 16-DEC-2013 / Unknown
#3) ALLOPURINOL (ALLOPURINOL) ; 16-DEC-2013 / Unknown
#4) AMLODIPINE (AMLODIPINE) ; 28-OCT-2014 / Unknown
#5) ATORVASTATINE /01326101/ (ATORVASTATIN) ; 16-APR-2014 / Unknown
#6) CALCIUM (CALCIUM) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Benign prostatic hyperplasia (Benign prostatic hyperplasia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2651469

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included hyperlipidemia since 27-Mar-2001, intermittent paroxysmal atrial fibrillation (initial diagnosis), extracranial macroangiopathy, benign prostatic hyperplasia, urinary tract infection and IgA nephropathy which led to renal failure diagnosed in 26-Nov-2007. The patient had no known drug hypersensitivities and had no history of drug dependence. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent and did not previously experience any thromboembolic event before treatment with Retacrit. The patient had no history of exposure to other biosimilar products. It was reported that the patient had previously received Retacrit (epoetin zeta, 4000 IE decreasing to 2000/week; route of administration not reported) for an unknown indication. Concomitant medications included ciprofloxacin, tamsulosin, Torasemid, allopurinol, atorvastatine, calcium 500, Osteotriol, candesartan, amlodipine, and clonidin. On 27-Jan-2014, the patient started to receive epoetin zeta (Retacrit, lot number: 3T002VE and 4V057V4, 2000 U/week, dose also reported as 45 IU/kg/week, subcutaneous) for renal anemia. On 14-Nov-2014, the patient received the last dose of Retacrit prior to the onset of the adverse event. On 19-Nov-2014, the patient experienced A.cerebri posterior infarction. On 20-Nov-2014, the patient was admitted through emergency as an inpatient in the stroke unit due to a left-sided visual field defect that had been present for approximately 24 hours. Neurological examination on admission was performed: a right-handed patient with no meningism was presented. Confrontational perimetry testing showed a left-sided visual field defect, with the remaining cranial nerves normal. MER moderately vigorous on both sides. No spastic signs. No paresis. No atrophies. Muscle tone normal all around. Normal sensitivity. Coordination of upper and lower extremities normal. Slightly insecure gait. No tendency to fall shown in Romberg test. No deviation in Unterberger step test. Lasegue test results negative for both signs. A psychological test indicated an alert patient oriented in all respects. No evidence of neuropsychological deficits. On the same day of 20-Nov-2014, investigations showed CRP at 0.5 mg/ dL (up to 0.5) and 3.6 mg/L (less than 5), estimated GFR (Acc. to CKD-EPI) at 8 mL/min (normal range not reported), leukocytes at 7.39 1E9/L (4.4-11.3), Hb at 11.4 g/dL (13.5-17.5), haemoglobin at 10.9 g/dL (13.5-18, erythrocytes at 3.7/pl (4.4-5.9) and 3.5 1E12/L (4.4-5.9), Hkt at 34 % (40-53), haematocrit at 32 % (42-50), thrombocytes at 137 x 1E9/L (150-400), MCV at 92 fl (82-98), Hb/E at 31 pg (27-33), MCHC at 33 (31-36), PT (Quick) at 91 % (70-120), PT (INR) at 1.1 (2.1-4.0), APTT at 29 sec (less than 36), fibrinogen acc to Clauss at 4.6 g/L (2.1-4.0) and TSH 2.69 mU/L (0.27-4.20). ECG on 20-Nov-2014 showed normal frequency sinus rhythm and left axis deviation. ECG monitoring showed SVES and VES, intermittent tachycardia and artefacts overlaps, P waves not always easily delimitable, sometimes arrhythmic. The patient received one time dose of Clexane (4000 IU, subcutaneous) and ASA (500 mg, intravenous) due to suspected cerebral ischemia; heparin (7500-0-7500; route of administration not reported) was also started. On the same day of 20-Nov-2014, the suspect drug was discontinued in response to the adverse event. It was unknown if the symptoms improved after the suspect drug was discontinued. On 21-Nov-2014, additional neurological diagnostics were performed and showed that during extracranial Doppler-/duplex sonography: taking into account the main and additional criteria, findings consistent with macroangiopathy with no evidence of localised stenoses (LE according to NASCET criteria 10%). N.B.: ACE stenosis on sides (left max. blood flow rate 190 cm/sec, right max. blood flow rate 188 cm/sec) and transcranial Doppler-/duplex sonography: normal findings for the left supratentorial and infratentorial. Right supratentorial findings consistent with a tandem stenosis (max. blood flow rate approx. 160 cm/sec). On the same day, transoesophageal echo (incl. large vessels) was also performed and showed AV: sclerosed, slight insufficiency, some stenoses, fibrous deposits a.e. degenerative genesis MV: sclerosed, slight to moderate insufficiency, no stenoses, small fibrous deposits, degenerative DD, torn tendons, LA with no thromboses, no spontaneous echo contrast, no evidence of thrombosis in LAA. Systolic LV function preserved, no evidence of an ASA. After administration of contrast agent, there was no transfer into LA, no atrial septal defect. On 25-Nov-2014, laboratory values showed , creatinine: 5.13 mg/dL, CRP at 3.1 mg/L, estimated GFR (acc. to CKD-EPI (2009)) at 9 mL/min, leukocytes at 7.94 x1E9/L, erythrocytes at 3.8 x 1E12/L, haemoglobin at 11.5 g/dL, haematocrit at 35 %, and thrombocytes at 161 x1E9/L. Treatment recommendations included : a secondary prophylaxis is initiated consisting of anticoagulant treatment with phenprocoumon for the renal insufficiency, commenced therapeutic dosing of marcumar under heparin on 26.11.2014 at 9mg /d and request dosing according to the scheme (6mg/d on 27-Nov-2014 and 3 mg/d on 28-Nov-2014) and continuation according to INR (target: 2.0 to 3.0), continuation of the existing medication with atorvastatin to stabilize plaque resulting from macroangiopathy and degenerative changes to the mitral and aortic valves. The antibiotic medication with ciprofloxacin being administered at the time of admission to treat a urinary tract infection can be stopped with declining inflammation parameters. The patient had ongoing monitoring of inflammation parameters and in particular retention values and serum electrolytes. Follow-up care of the visual field defect by an ophthalmologist was suggested and explained to the patient that his ability to drive would be impaired until further updates. The patient was registered for rehabilitation, which the patient will follow-up with at home. On 26-Nov-2014, the patient was discharged, still with loss of sight, hemianopsia left. On discharge, NIHSS clinical scale was 2 points (normal value not reported). On an unknown date, Retacrit was readministered. Also on an unknown date, the patient experienced myocardial infarction. Laboratory or diagnostic information, treatment and action taken with epoetin zeta in response to the event were not reported. On 09-Oct-2015, the patient died. Cause of death was myocardial infarction. An autopsy was not performed. The reporter's opinion of causality for the event of A.cerebri posterior infarction and epoetin zeta was probably yes. It was reported that Torasemid may also pose the patient at risk for thromboembolic events. Risk factors also included CKD III B and hypertension since 27-Mar-2001. The reporter's opinion of causality between the event of fatal myocardial infarction and epoetin zeta was not provided. 03-Dec-2014: Additional information was received regarding reporter details. This information has been incorporated in the corresponding data fields. 05-Dec-2014: Additional information was received from the same reporter. It was confirmed that the patient was enrolled in a Hospira-sponsored study. The patient's ethnicity, risk factors, and medical history were provided. Adverse event reported term was updated to A. cerebri posterior infarction. Doses, indications, frequencies and therapy dates of concomitant medications were provided. Brand name of calcitriol was

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

provided. Laboratory tests were provided. Treatment, outcome of the adverse event was provided. The reporter's causality assessment was updated to probably yes. An alternative etiology was provided. Life-threatening was added as a seriousness criterion. The reporter was able to provide the following information for identification and traceability of the biosimilar product Retacrit: Lot number, expiry date and previous exposure to other biosimilars. This information has been incorporated in the narrative and in the corresponding data fields. 12-Dec-2014: Additional information was received from the same reporter. Indication of calcium was updated to nutritional supplement. Illegible therapy year for amlodipine was updated to 2014. This information has been incorporated in the narrative and in the corresponding data fields. 16-Dec-2014: Additional information was received from the same reporter. Patient's date of birth was updated. Intermittent paroxysmal atrial fibrillation, extracranial macroangiopathy, benign prostatic hyperplasia and urinary tract infection were added as medical history. Ciprofloxacin was added as concomitant medication. Clexane and ASA were added as treatment for the adverse event. Treatment recommendations were provided. Neurological examinations and diagnostics, additional blood tests, ECG and imaging procedures were provided. This information has been incorporated in the narrative and in the corresponding data fields. 28-Oct-2015: Additional information was received from the same reporter. Fatal myocardial infarction was added as an adverse event. The patient also received Retacrit (lot number 4V057V4). This information has been incorporated in the narrative and in the corresponding data fields

Case Comment: Overall case causality: Possible Event is possibly related as the suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration. Consider also contributory effects of risk factors in the medical history, as patient likely has hypertension and dyslipidemia based on the concomitant medications being taken. Follow-up: No change in previous assessment. Follow-up: New information noted. Overall causality upgraded to probable given the reporter's causality. No change in previous company assessment. Follow-up: New information noted, but does not warrant change in previous causality assessment. Follow-up: New information noted, but does not warrant change in previous causality assessment. Follow-up: Overall case causality: Related No change in previous assessment, but causality is updated to related based on Hospira's binary causality assessment guidelines.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	20-NOV-2014	Activated partial thromboplastin time	29 seconds	
2	25-NOV-2014	Blood creatinine	5.13 mg/dl	1.10 0.5
3	20-NOV-2014	Blood fibrinogen	4.6 g/l	4.0 2.1
4	20-NOV-2014	Blood thyroid stimulating hormone	2.69 mU, Unknown	4.20 0.27
5	20-NOV-2014	C-reactive protein	0.5 mg/dl	
6	20-NOV-2014	C-reactive protein	3.6 mg/dl	
7	25-NOV-2014	C-reactive protein	3.1 mg/dl	
8	21-NOV-2014	Echocardiogram	No evidence of an ASA. After administration of,	
9	21-NOV-2014	Echocardiogram	septal defect., Unknown	
10	21-NOV-2014	Echocardiogram	stenoses, small fibrous deposits,degenerative DD,	
11	21-NOV-2014	Echocardiogram	torn tendons., Unknown	
12	21-NOV-2014	Echocardiogram	fibrous deposits a.e. degenerative genesis, Unkno	
13	21-NOV-2014	Echocardiogram	LA with no thromboses, no spontaneous echo,Unknown	
14	21-NOV-2014	Echocardiogram	AV: sclerosed, slight	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			insufficiency, some stenoses	
15	21-NOV-2014	Echocardiogram	contrast agent, no transfer into LA, no atrial, U	
16	21-NOV-2014	Echocardiogram	MV:sclerosed,slight to moderate insufficiency,no,	
17	21-NOV-2014	Echocardiogram	Systolic LV function preserved., Unknown	
18	21-NOV-2014	Echocardiogram	contrast, no evidence of thrombosis in LAA., Unkno	
19		Electrocardiogram	sometimes arrhythmic, Unknown	
20		Electrocardiogram	SVES and VES, intermittent tachycardia and,Unknown	
21		Electrocardiogram	artefacts overlaps,P waves not easily delimitable,	
22	20-NOV-2014	Electrocardiogram	Normal frequency sinus rhythm.Left axis deviation,	
23	20-NOV-2014	Glomerular filtration rate	8 ml/min	
24	25-NOV-2014	Glomerular filtration rate	9 ml/min	
25	20-NOV-2014	Haematocrit	34 %	53 40
26	20-NOV-2014	Haematocrit	32 %	50 42
27	25-NOV-2014	Haematocrit	35 %	50 42
28	20-NOV-2014	Haemoglobin	10.9 g/dl	18.0 13.5
29	20-NOV-2014	Haemoglobin	11.4 g/dl	17.5 13.5
30	25-NOV-2014	Haemoglobin	11.5 g/dl	18.0 13.5
31	20-NOV-2014	Haemoglobin E	31 pg	33 27
32	20-NOV-2014	International normalised ratio	1.1, Unknown	4.5 2.0
33	20-NOV-2014	Lasegue's test	Negative for both signs, Unknown	
34	20-NOV-2014	Mean cell haemoglobin concentration	33 g/dl	36 31
35	20-NOV-2014	Mean cell volume	92 FL	98 82
36	20-NOV-2014	Neurological examination	Normal, Unknown	
37	20-NOV-2014	Neurological examination	Moderately vigorous on both sides, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
38	20-NOV-2014	Neurological examination	Normal, Unknown	
39	20-NOV-2014	Neurological examination	Slightly inecure, Unknown	
40	20-NOV-2014	Neurological examination	Normal all around, Unknown	
41	20-NOV-2014	Neurological examination	Right handed patient with no meningism, Unknown	
42	20-NOV-2014	Neuropsychological test	Alert patient oriented in all respects, Unknown	
43	20-NOV-2014	Neuropsychological test	No evidence of neuropsychological deficits,Unknown	
44	20-NOV-2014	Platelet count	137 x 1E9, Unknown	400 150
45	25-NOV-2014	Platelet count	161 x 1E9, Unknown	400 150
46	20-NOV-2014	Prothrombin time	91 %	120 70
47	20-NOV-2014	Red blood cell count	3.5 x 1E12, Unknown	5.9 4.5
48	20-NOV-2014	Red blood cell count	3.7/pl, Unknown	5.9 4.4
49	25-NOV-2014	Red blood cell count	3.8 x 1E12, Unknown	5.9 4.5
50	20-NOV-2014	Romberg test	No tendency to fall, Unknown	
51	20-NOV-2014	Sensory level	Normal, Unknown	
52	21-NOV-2014	Ultrasound Doppler	infratentorial.Right supratentorial findings, Unk	
53	21-NOV-2014	Ultrasound Doppler	rate approx. 160 cm/sec), Unknown	
54	21-NOV-2014	Ultrasound Doppler	Macroangiopathy, no evidence local stenoses, Unk	
55	21-NOV-2014	Ultrasound Doppler	Rmax. blood flow rate 188 cm/sec), Unknown	
56	21-NOV-2014	Ultrasound Doppler	consistent with a tandem stenosis (max. blood flo	
57	21-NOV-2014	Ultrasound Doppler	LE according to NASCET criteria 10%, Unknown	
58	21-NOV-2014	Ultrasound Doppler	ACE stenosis both sides (Lmax. blood flow rate, U	
59	21-NOV-2014	Ultrasound Doppler	normal findings for the left supratentorial and,	
60	20-NOV-2014	Vestibular function test	No deviation, Unknown	
61	20-NOV-2014	Visual field tests	Left-sided visual field defect, Unknown	
62	26-NOV-2014	Visual field tests	Left-sided visual field no other focal deficits,	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
63	20-NOV-2014	White blood cell count	7.39 x 1E9, Unknown	11.3 4.4
64	25-NOV-2014	White blood cell count	7.94 x 1E9, Unknown	11.3 4.4

13. Relevant Tests

Confrontational perimetry testing(26Nov2014): Left-sided visual field no other focal deficits, Unknown.
ECG (20Nov2014): Normal frequency sinus rhythm.Left axis deviation, Unknown
ECG Monitoring (Unknown date): artefacts overlaps,P waves not easily delimitable, Unknown
Extracranial Doppler-/duplex sonography (21Nov2014): ACE stenosis both sides (Lmax. blood flow rate, Unknown
Extracranial Doppler-/duplex sonography (21Nov2014): Macroangiopathy, no evidence local stenoses ,Unknown
Transcranial Doppler-/duplex sonography (21Nov2014): consistent with a tandem stenosis (max. blood flow ,Unknown
Transcranial Doppler-/duplex sonography (21Nov2014): normal findings for the left supratentorial and ,Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): AV: sclerosed, slight insufficiency,some stenoses, Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): contrast agent, no transfer into LA, no atrial, Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): contrast, no evidence of thrombosis in LAA., Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): fibrous deposits a.e. degenerative genesis, Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): MV:sclerosed,slight to moderate insufficiency,no, Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): No evidence of an ASA. After administration of , Unknown
Transoesophageal echo (incl. largevessels) (21Nov2014): stenoses, small fibrous deposits,degenerative DD, , Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3T002V3; Exp.Dt. 01-DEC-2015}; Regimen #1	2000 U, Solution for injection in pre-filled syringe, Freq: 1 Week; Interval 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	27-JAN-2014 / 20-NOV-2014; 298 days
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4V057V4; Exp.Dt. 01-AUG-2017}; Regimen #2	2000 U, Solution for injection in pre-filled syringe, Freq: 1 Week; Interval 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	27-JAN-2014 / 20-NOV-2014; 298 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) CANDESARTAN (CANDESARTAN) ; 28-FEB-2012 / Unknown

#8) CIPROFLOXACIN (CIPROFLOXACIN) ; Unknown

#9) CLONIDIN (CLONIDINE HYDROCHLORIDE) ; 04-NOV-2014 / Unknown

#10) TAMSULOSIN (TAMSULOSIN) ; 29-SEP-2012 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Medical history included hyperlipidemia since 27-Mar-2001, intermittent paroxysmal atrial fibrillation (initial diagnosis), extracranial macroangiopathy, benign prostatic hyperplasia, urinary tract infection and IgA nephropathy which led to renal failure diagnosed in 26-Nov-2007 . The patient had no known drug hypersensitivities and had no history of drug dependence. The patient was not on dialysis. The patient was not treated with an erythropoiesisstimulating agent and did not previously experience any thromboembolic event before treatment with Retacrit. The patient had no history of exposure to other biosimilar products. It was reported

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		that the patient had previously received Retacrit (epoetin zeta, 4000 IE decreasing to 2000/week; route of administration not reported) for an unknown indication. Tobacco usage and alcohol consumption were not reported. Risk factors also included CKD III B also reported as chronic renal insuffiiciency and hypertension since 27-Mar-2001. Race/ Ethnicity: Caucasian On 09-Oct-2015, the patient died. Cause of death was myocardial infatction. An autopsy was not performed.
Unknown to Ongoing	Relevant Med History	Macroangiopathy (Macroangiopathy);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	IgA nephropathy (IgA nephropathy);
Unknown to Ongoing	Relevant Med History	Paroxysmal atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Urinary tract infection (Urinary tract infection);
Unknown	Relevant Med History	Chronic kidney disease (Chronic kidney disease);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Past Drug Event Lot number: UNK	Epoetin Zeta (EPOETIN ZETA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	22	FEB	1931	83 Years	Female	65.00 kg	04	NOV	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cerebral stroke [Cerebrovascular accident]

Case Description: Fatal cerebral stroke. Epoetin zeta Serious Hospira sponsored clinical study report from Italy, received from an investigator (reference: It-120-0019) which refers to an 83-year-old Caucasian female patient (weight: 75 kg and height: 163
cm). This case was also received from AIFA (ref: IT-MINISAL02-285956). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 15-DEC-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 5000 IU, 7 (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 22-NOV-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPINE (AMLODIPINE) Capsule ; Unknown
#2) CLONIDINE (CLONIDINE) Capsule ; Unknown
#3) METOPROLOL (METOPROLOL) Capsule ; Unknown
#4) ROSUVASTATIN (ROSUVASTATIN) ; Unknown
#5) SERTRALINE (SERTRALINE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic gastritis (Chronic gastritis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2653522

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-MAY-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

subcutaneously for the treatment of renal anaemia. Medical history included hypertensive nephropathy which led to renal failure on 15-Jan-2011, ischemic heart disease and chronic gastritis. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. The patient had no previous exposure to other biosimilars. Concomitant medications included amlodipine (5 mg, 1 cap/day, oral), metoprolol (100 mg 1 cap/day, oral), clonidine (150 mcg, 1 cap/day, oral) for hypertension; rosuvastatin (10 mg, oral) for hyperlipidemia; and sertraline (50 mg, oral) for cerebrovascular disease. On 22-Nov-2011, the patient began treatment with Retacrit (epoetin zeta, 5000 IU, 76 IU/kg/week, once a week, subcutaneous; lot number was unknown) for renal anaemia. On 14-Jul-2014, PTH result showed 101.6 pg/ml (N: 12.0 - 65.9). On 01-Nov-2014, the patient received last dose prior to event. On 04-Nov-2014, the patient experienced cerebral stroke described as progressive lack of force and disorder of speech. The patient has been hospitalized on 04-Nov-2014 due to cerebral stroke. Treatment for the adverse event was unknown. After 40 days, the patient died in the hospital. Action taken with epoetin zeta was not applicable. On 15-Dec-2014, the patient died. Cause of death was cerebral stroke. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event of cerebral stroke and epoetin zeta was unlikely. Risk factors included myocardial infarction, cerebrovascular disease, hyperlipidemia, hypertension and diabetes type 2. 04-Feb-2015: Corrected report was created to reflect routes of administration of amlodipine, metoprolol, clonidine, rosuvastatin, and sertraline. This information has been incorporated in the narrative and in the corresponding data fields. 11-May-2015: Additional information was received from the same reporter. Adverse event has been updated from ischemic stroke to cerebral stroke. It was reported that the patient died on 15-Dec-2014. Date of hospitalization has been added. Causality assessment has been updated from not related to unlikely. Life-threatening has been added as a seriousness criteria. This information has been incorporated in the narrative and in the corresponding data fields. 22-May-2015: Corrected report was created to update the patient's year of death from 2015 to 2014 in the narrative and in the corresponding data field. 28-May-2015: English translation of laboratory test result was received. PTH result has been added. This information has been incorporated in the narrative and in the corresponding data field.

Case Comment: Overall case causality: Possible Event is possibly related as the suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration. Consider also contributory effects from multiple preexistent cardiovascular risk factors. Follow-up: Overall case causality: Related New information noted. Causality updated to Related to align with company's new binary causality assessment. Patient had been on the drug for more than three years, and Retacrit can theoretically increase the risk of thromboembolic events. Follow-up: No change in previous assessment. Corrected report: No change in previous assessment. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	14-JUL-2014	Blood parathyroid hormone	101.6 PG/ML	65.9 12.0

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	5000 IU, 76 IU/kg/week, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	22-NOV-2011 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption and tobacco usage were not reported. Medical history included hypertensive nephropathy which led to renal failure on 15-Jan-2011, hyperlipidemia, ischemic heart disease, hypertension, chronic vasculitis, and cerebrovascular disease. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. The patient had no previous exposure to other biosimilars. Race/Ethnicity: Caucasian On 15-Dec-2014, the patient died. Cause of death was cerebral stroke. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);

Mfr. Control Number: 2653522

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy); Diagnosed on 15-Jan-2011
Unknown	Relevant Med History	Unspecified cerebrovascular disease (Cerebrovascular disorder);
Unknown	Relevant Med History	Type II diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	30	DEC	1936	77 Years	Male	Unk	29	OCT	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]
Cardiac arrest [Cardiac arrest]

Case Description: Fatal acute myocardial infarction and fatal cardiac arrest. Epoetin zeta. Serious Hospira-sponsored study report from Greece, received from an investigator (reference: Gr-002-0019), which refers to a 78-year-old male Caucasian patient
(height: 156 cm, dry weight: 52 kg). The patient had no history of allergies, drug hypersensitivities, drug dependence, and no history of alcohol consumption.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 31-OCT-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 96.15 iu/kg (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 19-MAY-2014 / 29-OCT-2014

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATORVASTATIN (ATORVASTATIN) ; 01-JAN-2005 / 31-OCT-2014
#2) CLOPIDOGREL (CLOPIDOGREL) ; 01-JAN-2007 / 31-OCT-2014
#3) METOPROLOL (METOPROLOL) ; 01-JAN-2010 / 31-OCT-2014

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Breathlessness (Dyspnoea)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2693195

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-JAN-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was an ex-smoker of 3 packets per day, where he stopped in 2005. The patient had diabetic nephropathy which led to renal failure diagnosed on 01-Apr-2014. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit, and the patient did not receive Retacrit before the study. Patient's medical history also included coronary heart disease, myocardial infarction, ischemic heart failure also reported as ischemic heart disease since 2005, cardiac pacing, diabetes mellitus and hypertension both since 2000, and bypass surgery. The patient was not exposure to other biosimilar products aside from Retacrit. Concomitant medications included clopidogrel (75 mg, once per day) for coronary heart disease, atorvastatin (10 mg, once per day) and metoprolol (100 mg, 1/4 twice per day), both given for myocardial infarction. The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. On 19-May-2014, the patient began treatment with Retacrit (epoetin zeta; 96.15 iu/kg/week, 1 dosage per week ; dose also reported as 13.735 iu/kg/day; subcutaneous, solution for injection in pre-filled syringe; lot number and date of expiry not available, strength unknown) for renal anaemia. On 20-Sep-2014, complete blood count showed red blood cells of 4.74 M/mcl (normal range: 4.50 to 5.90), haemoglobin of 11.1 g/dl (normal range: 13.5 to 17.5), haematocrit of 37.2 % (normal range: 41.0 to 53.0), mean cell volume of 78.5 fl (normal range: 76.0 to 96.0), mean cell haemoglobin of 23.4 pg (normal range: 27.0 to 33.0), mean cell haemoglobin concentration of 29.8 g/dl (normal range: 30.0 to 36.0), RBC distribution width of 18.7 % (normal range: 11.0 to 16.0), distribution width – standard deviation of 51.3 fl (normal range: 38.0 to 43.0), white blood cell count of 6.70 K/mcl (normal range: 4.00 to 11.00), neutrophils of 55.8 % (normal range: 40.0 to 75.0), lymphocytes of 12.5 % (normal range:20.0 to 40.0), monocytes of 29.4 % (normal range: 2.0 to 10.0) and eosinophils of 0.7 % (normal range: 1.0 to 6.0). On 20-Oct-2014, complete blood count revealed red blood cells of 4.14 M/mcl, haemoglobin of 9.9 g/dl, haematocrit of 32.1 %, mean cell volume of 77.5 fl, mean cell haemoglobin of 23.9 pg, mean cell haemoglobin concentration of 30.8 g/dl, RBC distribution width of 20.9 %, distribution width – standard deviation of 56.4 fl, white blood cell count of 8.28 K/mcl, neutrophils of 66.3 %, lymphocytes of 5.9 %, monocytes of 27.7 % and eosinophils of 0.0 %. On 29-Oct-2014, the patient experienced acute myocardial infarction, also described as heart attack; and cardiac arrest. The patient also had low blood pressure and breathlessness. Treatment for the events included monitoring and tracheal intubation. On the same day of 29-Oct-2014, epoetin zeta was discontinued in response to the adverse events but the symptoms did not improve. Other laboratory and diagnostic tests are not available. It was also reported that there are no relevant test or laboratory data. On 31-Oct-2014, after a duration of 3 days, the patient died. Causes of death were cardiac arrest and acute myocardial infarction. No autopsy was performed. The reporter's opinion of causality for the event fatal cardiac arrest and acute myocardial infarction in relation to epoetin zeta was not related. Risk factors included coronary heart disease, myocardial infarction, peripheral arterial disease, hyperlipidaemia, hypertension, diabetes type 2 with diabetic vascular complications, heart failure NYHA stage III, and smoking. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: lot number and date of expiry. 15-Jan-2015: Additional information was received from the reporter. The updated events are fatal acute myocardial infarction and fatal cardiac arrest. History of allergies and alcohol consumption, history of biosimilar exposure, autopsy information, and reporter's causality assessment were updated. The patient's date of birth was also reported as 30-Jan-1936 (previously reported as 30-Dec-1936). Data entry corrections were made to reflect the patient's age; to reflect that the outcome of the event acute myocardial infarction was fatal; to reflect the onset date of the events as 29-Oct-2014, and their duration as 3 days; to reflect the treatment for the events; to reflect the other manifestations of the events; to reflect the events as life threatening; to reflect the action taken with Retacrit; to reflect the concomitant medications. These information were reflected in the narrative and in the corresponding data fields. 26-Jan-2015: Corrected report was created to reflect updates received on 15-Jan-2015 which were truncated in the previous report. 27-Jan-2015: English translation of the Danish text has been received. Complete blood count results were included. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Cannot provide causation of events without firm timeline (including onset date of adverse events), patient age, a more detailed medical history including cardiovascular risk factors, and concomitant medications, if any. - N. Gonzales (06 Jan 2015) Follow-up: Overall case causality: Not related New information noted. Though the suspect drug can theoretically increase the risk of thromboembolic events, the patient's underlying cardiovascular risk factors far outweigh the risk from the drug. Patient had preexistent coronary artery disease since 2005 and has other risk factors such as hyperlipidemia, hypertension and diabetes. - N. Gonzales (23 Jan 2015) Corrected report: No change in previous causality assessment. - N. Gonzales (26 Jan 2015) Follow-up: No change in previous causality assessment. - N. Gonzales (04 Feb 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood pressure measurement	low, Unknown	
2	20-SEP-2014	Eosinophil count	0.7 %	6.0 1.0
3	20-OCT-2014	Eosinophil count	0.0 %	6.0 1.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
4	20-SEP-2014	Haematocrit	37.2 %	53.0 41.0
5	20-OCT-2014	Haematocrit	32.1 %	53.0 41.0
6	20-SEP-2014	Haemoglobin	11.1 g/dl	17.5 13.5
7	20-OCT-2014	Haemoglobin	9.9 g/dl	17.5 13.5
8	20-SEP-2014	Lymphocyte count	12.5 %	40.0 20.0
9	20-OCT-2014	Lymphocyte count	5.9 %	40.0 20.0
10	20-SEP-2014	Mean cell haemoglobin	23.4 pg	33.0 27.0
11	20-OCT-2014	Mean cell haemoglobin	23.9 pg	33.0 27.0
12	20-SEP-2014	Mean cell haemoglobin concentration	29.8 g/dl	36.0 30.0
13	20-OCT-2014	Mean cell haemoglobin concentration	30.8 g/dl	36.0 30.0
14	20-SEP-2014	Mean cell volume	78.5, FL	96.0 76.0
15	20-OCT-2014	Mean cell volume	77.5, FL	96.0 76.0
16	20-SEP-2014	Monocyte count	29.4 %	10.0 2.0
17	20-OCT-2014	Monocyte count	27.7 %	10.0 2.0
18	20-SEP-2014	Neutrophil count	55.8 %	75.0 40.0
19	20-OCT-2014	Neutrophil count	66.3 %	75.0 40.0
20	20-SEP-2014	Red blood cell count	4.74 M/mcl, Unknown	5.90 4.50
21	20-OCT-2014	Red blood cell count	4.14 M/mcl, Unknown	5.90 4.50
22	20-SEP-2014	Red cell distribution width	18.7 %	16.0 11.0
23	20-SEP-2014	Red cell distribution width	51.3, FL	43.0 38.0
24	20-OCT-2014	Red cell distribution width	56.4, FL	43.0 38.0
25	20-OCT-2014	Red cell distribution width	20.9 %	16.0 11.0
26	20-SEP-2014	White blood cell count	6.70 K/mcl, Unknown	11.00 4.00
27	20-OCT-2014	White blood cell count	8.28 K/mcl, Unknown	11.00 4.00

Mfr. Control Number: 2693195

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	96.15 iu/kg/week, Freq: 1 Week; Interval:1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	19-MAY-2014 / 29-OCT-2014; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient had no history of allergies, drug hypersensitivities, drug dependence, and no history of alcohol consumption. The patient was an ex-smoker of 3 packets per day, where he stopped in 2005. The patient had diabetic nephropathy which led to renal failure diagnosed on 01-Apr-2014. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit, and the patient did not receive Retacrit before the study. Patient's medical history also included coronary heart disease, myocardial infarction, ischemic heart failure also reported as ischemic heart disease since 2005, cardiac pacing, diabetes mellitus and hypertension both since 2000, and bypass surgery. The patient was not exposure to other biosimilar products aside from Retacrit. Risk factors included coronary heart disease, myocardial infarction, peripheral arterial disease, hyperlipidaemia, hypertension, diabetes type 2 with diabetic vascular complications, heart failure NYHA stage III, and smoking. Race/Ethnicity: Caucasian On 31-Oct-2014, after a duration of 3 days, the patient died. Causes of death were cardiac arrest and acute myocardial infarction. No autopsy was performed.
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History Since 2005	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Low blood pressure (Hypotension);
Unknown to Ongoing	Relevant Med History 01-Apr-2014	Renal failure (Renal failure);
Unknown	Relevant Med History	Bypass surgery (Vascular graft);
Unknown	Relevant Med History	Cardiac pacemaker insertion (Cardiac pacemaker insertion);
Unknown	Relevant Med History Risk Factor	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History Risk Factor	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor-3 packs per day, stopped in 2005	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History Risk Factor	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History Risk Factor	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Risk Factor	
Unknown	Relevant Med History Risk Factor	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History Risk Factor	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Abstains from alcohol (Abstains from alcohol);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	MAR	1936	78 Years	Male	103.40 kg	01	SEP	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pulmonary artery embolism [Pulmonary embolism]

Case Description: Fatal pulmonary artery embolism. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from a physician (ref: Ge-471-0015) which refers to a 78-year-old Caucasian male patient (dry weight: 103.4 kg; height: 180
cm, also reported as 178). The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 09-DEC-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 58 IU/kg, Freq:1 week, INterval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal Anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 31-JUL-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FALITHROM (PHENPROCOUMON) ; Unknown
#2) FURORESE /00032601/ (FUROSEMIDE) ; Unknown
#3) GLUCOBAY (ACARBOSE) ; Unknown
#4) HYDROCHLOROTHIAZIDE (HYDROCHLOROTHIAZIDE) ; Unknown
#5) LOESFERRON (FERROUS GLUCONATE) ; Unknown
#6) METOPROLOL (METOPROLOL) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2715463

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2715463

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

coronary artery sclerosis, heart failure and chronic kidney disease. The patient had no known drug hypersensitivities and no history of drug dependence. Concomitant medications included ramipril Hexal 5 mg (2 x 1/2 unit daily or 1/2 unit in the morning and 1/2 unit in the evening), Falithrom (acc to value, daily), furosemide 125 1A Pharma (1 x 1 unit, daily), sildenafil 20 mg (Revatio, 2 x 1 unit daily or 1 in the morning and 1 in the evening), pantoprazol 1A Pharma 40 mg (1 x 1 unit in the morning daily), metoprolol 95 mg (Metohexal-Succ, 2 x 1 unit daily or 1 in the morning and 1 in the evening), hydrochlorothiazide 25 mg (HCT Hexal, 1 x 1 unit daily), Furorese 125 mg (1 unit daily 1/2 h before breakfast), Loesferron (1 unit daily), Glucobay 100 (1 unit in the morning, noon and evening), Nephrotrans 840 mg (1 unit in the morning and in the evening) (all given orally) and warfarine (INR 2.5, route of administration not reported) all were given for unknown indications. On 31-Jul-2012, the patient started treatment with Retacrit (epoetin zeta, 58 IU/kg, one dosage per week, dose also reported as 8000 IE/week, subcutaneous; lot number not reported) for renal anaemia. It was reported that the patient was enrolled in the study on 28-May-2014. On an unknown day in Sep-2014, the patient experienced pulmonary artery embolism with decompensated cor pulmonale as a differential diagnosis. The last haemoglobin value of the patient was 6.4 mmol/L (normal values not reported), hence polyglobulia can be excluded. Treatment for the adverse event and action taken with epoetin zeta in response to the event were not reported. The patient died on 09-Dec-2014 in a hospital. Cause of death was pulmonary artery embolism. It was not reported if an autopsy was performed. The reporter's opinion of causality for the event of fatal pulmonary artery embolism in relation to Retacrit was unlikely. Risk factors included diabetes type 2 with no vascular complications. 07-Sep-2015: Additional information received from the same reporter. The patient's age, medical history and concomitant medications; event onset date, laboratory test and reporter's causality for the event were provided. The height of the patient was also reported as 178 cm. It was reported that decompensated cor pulmonale was used as a differential diagnosis. It was also reported that the patient died in a hospital. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number, date of expiry and previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Although the suspect drug can theoretically increase the risk of thromboembolic events by mechanism of action, cannot provide without firm timeline objective clinical event details, medical history and concomitant medications. Patient also has confounding risk factor of diabetes. Follow-up: Overall case causality: Related Possible contributory effect of the suspect drug - as it does increase the risk of thromboembolic events, but consider also other pre-existing and predisposing risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	6.4 mmol/l	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) NEPHROTRANS (SODIUM BICARBONATE) ; Unknown

#8) RAMIPRIL HEXAL (RAMIPRIL) ; Unknown

#9) SILDENAFIL (SILDENAFIL) ; Unknown

#10) FUROSEMIDE (FUROSEMIDE) ; Unknown

#11) PANTOPRAZOLE (PANTOPRAZOLE) ; Unknown

#12) WARFARINE (WARFARIN) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. Medical history included coronary artery sclerosis, heart failure and chronic kidney disease. The patient had no known drug hypersensitivities and no history of drug dependence. Race/Ethnicity: Caucasian. Cause of death was pulmonary artery embolism. It was not reported if an autopsy was performed. Risk factors included diabetes

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	type 2 with no vascular complications.	
Unknown to Ongoing	Relevant Med History	Coronary artery sclerosis (Arteriosclerosis coronary artery);
Unknown to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	21	SEP	1927	87 Years	Female	56.00 kg	06	JAN	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Hip fracture [Hip fracture]
Pulmonary embolism [Pulmonary embolism]

Case Description: Fatal pulmonary embolism, hip fracture. Epoetin zeta. Serious Hospira-sponsored study report from Greece, received from an investigator (reference: Gr-045-0026), which refers to an 87-year-old Caucasian female patient (weight: 56 kg,
height: 158 cm). The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 14-JAN-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 99 IU/kg, Freq:1 week, Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 21-JUL-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FUROSEMIDE (FUROSEMIDE) ; 15-NOV-2014 / 06-JAN-2015
#2) PERINDOPRIL (PERINDOPRIL) ; 30-JUL-2014 / 06-JAN-2015

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2737056

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-MAR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had no known drug hypersensitivities or history of drug dependence. Patient's medical history included hypertensive nephropathy which led to renal failure diagnosed on 15-Jul-2014. The patient was not on dialysis, was not treated with an erythropoiesis-stimulating agent (ESA), and has not received Retacrit prior to the study. Concomitant medications included furosemide (60 mg) and perindropil (5 mg) (once daily; routes of administration were not reported); both given for hypertension. On 15-Jul-2014, patient's hemoglobin was 8.75, hematocrit was 28.3, platelet count was 135 (unit of measurements and normal values were not reported), heterozygous beta-thalassaemia minor was noted. On 21-Jul-2014, the patient started treatment with Retacrit (epoetin zeta, 99 IU/kg/week, 1 dosage/week, subcutaneous; lot number unknown) for renal anaemia. On the same day of 21-Jul-2014, hemoglobin was 8.7, hematocrit was 28.1, and platelet count was 155. On 30-Jul-2014, hemoglobin of 10.7, hematocrit of 34, and platelet count of 159. On 11-Sep-2014, hemoglobin was 11.2 and hematocrit of 35.1. On 04-Nov-2014, hemoglobin was 10.3, hematocrit was 32.8, and platelet count was 219. And on 20-Nov-2014, hemoglobin was 10, hematocrit was 32.9, and platelet count was 252. On 06-Jan-2015, the patient experienced hip fracture. It was reported that the patient was admitted to a hospital on the same day because of the adverse event and revealed hemoglobin of 11.7, hematocrit of 36.6, and platelet count of 251. On an unknown date, the patient developed pulmonary embolism. Treatment for the adverse events and action taken with the suspect drug were not reported. Outcome of the event of hip fracture was recovered on an unknown date. On 14-Jan-2015, the patient died. Cause of death was pulmonary embolism. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event of fatal pulmonary embolism and the suspect drug epoetin zeta was not reported while it was not related for the event of hip fracture. Risk factors included hypertension and diabetes mellitus type 2.
The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 12-Feb-2015: Additional information was received from the investigator. Laboratory results were added. This information has been incorporated in the narrative and corresponding data fields. Data entry correction was also made in the narrative to correct the subject number from Ge-045-0026 to Gr-045-0026. 25-Mar-2015: Additional information was received from the investigator. Hip fracture was deleted as cause of death. Outcome of the event of hip fracture was updated to recovered. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Possible (reporter causality not provided for pulmonary embolism) Hospira causality: Not related The pelvic fracture is not related and likely due to physical trauma. There is no plausible mechanism to implicate the suspect drug in this type of injury based on known mechanism of action. The pulmonary embolism is likewise not related, as this is a known complication of the underlying fracture. While the suspect drug can theoretically increase the risk of thromboembolic events, the underlying comorbidities and risk factors (post-fracture complication, hypertension, diabetes) far outweigh the potential risk from the drug. - N. Gonzales (11 Feb 2015) Follow-up: No change in previous causality assessment. - N. Gonzales (20 Feb 2015) Follow-up (02 Apr 2015): No change in previous causality assessment. - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit		
2	15-JUL-2014	Haematocrit	28.3, Unknown	
3	21-JUL-2014	Haematocrit	28.1, Unknown	
4	30-JUL-2014	Haematocrit	34, Unknown	
5	11-SEP-2014	Haematocrit	35.1, Unknown	
6	04-NOV-2014	Haematocrit	32.8. Unknown	
7	20-NOV-2014	Haematocrit	32.9, Unknown	
8	06-JAN-2015	Haematocrit	36.6, Unknown	
9	15-JUL-2014	Haemoglobin	8.75, Unknown	
10	21-JUL-2014	Haemoglobin	8.7, Unknown	
11	30-JUL-2014	Haemoglobin	10.7, Unknown	

Mfr. Control Number: 2737056

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
12	11-SEP-2014	Haemoglobin	11.2, Unknown	
13	04-NOV-2014	Haemoglobin	10.3, Unknown	
14	20-NOV-2014	Haemoglobin	10, Unknown	
15	06-JAN-2015	Haemoglobin	11.7, Unknown	
16	15-JUL-2014	Platelet count	135, Unknown	
17	21-JUL-2014	Platelet count	155, Unknown	
18	30-JUL-2014	Platelet count	159, Unknown	
19	04-NOV-2014	Platelet count	219, Unknown	
20	20-NOV-2014	Platelet count	252, Unknown	
21	06-JAN-2015	Platelet count	251, Unknown	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Tobacco usage and alcohol consumption were not reported. The patient had no known drug hypersensitivities or history of drug dependence. Patient's medical history included hypertensive nephropathy which led to renal failure diagnosed on 15-Jul-2014. The patient was not on dialysis, was not treated with an erythropoiesis-stimulating agent (ESA), and has not received Retacrit prior to the study. On 14-Jan-2015, the patient died. Cause of death was pulmonary embolism. It was not reported if an autopsy was performed. Risk factors included hypertension and diabetes mellitus type 2. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History Risk Factor	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	04	JAN	1929	85 Years	Male	68.00 kg	20	MAR	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cerebrovascular event [Cerebrovascular disorder]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 20-MAR-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 23-JAN-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DIFIX (CALCITRIOL) ; Unknown
#2) LASIX /00032601/ (FUROSEMIDE) Tablet ; Unknown
#3) SIMVASTATIN (SIMVASTATIN) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History leading to renal failure	Hypertensive nephropathy (Hypertensive nephropathy)
Unknown to Ongoing	Relevant Med History first diagnosed in 2001	Renal failure (Renal failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2789600

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-NOV-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Fatal cerebrovascular event. Epoetin zeta. Serious Hospira sponsored study report from Italy, received from a physician (ref: It-116-0024) which refers to an 85-year-old Caucasian male patient (dry weight: 68 kg; height: 160 cm). The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anemia. The patient had ongoing hypertensive nephropathy leading to renal failure (first diagnosed in 2001). The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications were not reported. On 23-Jan-2014, the patient started treatment with Retacrit (epoetin zeta, 58.8 IU/kg/week, 1 dosage per week, subcutaneous; lot number not reported) for renal anaemia. On an unknown date, the patient experienced cerebrovascular event. Laboratory/diagnostic tests, treatment for the adverse event and action taken with epoetin zeta in response to the event were not reported. The patient died on 20-Mar-2014. Cause of death was cerebrovascular event. It was not reported if an autopsy was performed. The reporter stated that the adverse event was considered not related to epoetin zeta but due to the patient's general conditions (i.e. old age and concomitant diseases). Risk factors included peripheral arterial disease, hypertension and being a current smoker. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: lot number, date of expiry, previous exposure of patient to other biosimilars. 27-Mar-2015: Additional information received from the investigator via AIFA. Reporter's causality was updated to not related (previously not reported) as event was due to the patient's general conditions (i.e. old age and concomitant diseases). This information has been incorporated in the narrative and corresponding data field.

Follow-up (21Nov2016): New reported information includes: The investigator reported that the patient was not exposed to any other ESA at any time. The patient did not experience any thrombolic event during treatment with any other ESA. The patient had not have risk factors for thrombembolic events, exception was smoking. Relevant concurrent disease were ongoing hypertension and ongoing peripheral arterial disease. Concomitant medications included calcitriol (DIFIX) 0.25 ug, once daily, furosemide (LASIX) 500 mg, 1/4 tablet weekly, simvastatin 20 mg, once daily. Not available was reported for laboratory /diagnostic results, diagnostic procedure, cerebrovascular accident and pulmonary embolism diagnostic tests results. The date of last dose prior to the event was reported as 20Mar2014. Mean dose applied within the period of 3 months prior to the event was 4000 IU/week. There had not been any dose changes within 3 months prior to the event. Event cerebrovascular event start date was 20Mar2014 with outcome of fatal. Hemoglobin was 10.7 g/dl.

Case Comment: In agreement with the reporting physician, the Company considered there was not a reasonable possibility that the reported event, cerebrovascular event, was related to epoetin zeta therapy. The event was most likely due to the subject's concurrent or underlying conditions. Elderly age, tobacco use and underlying disease of hypertension and peripheral arterial disease were predisposing factors in causing the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	10.7 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History Risk factor	Smoker (Tobacco user);
Unknown to Ongoing	Relevant Med History Risk factor	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History Risk factor	Peripheral arterial disease (Peripheral arterial occlusive disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	12	NOV	1937	Unk	Male	88.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cerebral Haemorrhage [Cerebral haemorrhage]

Case Description: Fatal cerebral haemorrhage. Epoetin zeta. Serious Hospira-sponsored study report from Italy, received from a physician (ref: It-090-0022) which refers to a Caucasian male patient (dry weight: 88 kg; height: 178 cm; age not reported). This
report was also received from AIFA (ref: IT-MINISAL02-300957). The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 07-APR-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 134 IU/kg/ (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal Anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 29-APR-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2791899

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-AUG-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2791899

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had diabetic nephropathy which led to renal failure (first diagnosed on 22-Feb-2012) and was receiving renal dialysis since 10-Jan-2014 with an average of three dialysis per week. The patient had not received any other erythropoietin stimulating agents (ESA) before treatment with Retacrit. The patient had peripheral vascular disease. Concomitant medications were not reported. On 29-Apr-2013, the patient began treatment with Retacrit (epoetin zeta, 134 IU/kg/week, three dosages per week, subcutaneous, lot number not reported) for renal anaemia. The patient was enrolled in the study on 31-Jan-2014. On an unknown date, the patient experienced cerebral haemorrhage. Laboratory/ diagnostic tests and treatment for the adverse event were not reported. Action taken with the suspect drug in response to adverse event was not reported. The patient died on 07-Apr-2014. Cause of death was reported as cerebral haemorrhage. It was not reported if an autopsy was performed. The reporter's opinion of causality for the event of fatal cerebral haemorrhage in relation to Retacrit was not related. Risk factors included peripheral arterial disease, hypertension, diabetes type 2 with diabetic vascular complications. 11-Aug-2015: Additional information was received from AIFA (Ref: IT-MINISAL02-3009527) to update the event term to fatal cerebral haemorrhage (previously reported as fatal cerebral hemorragy). Peripheral vascular disease was added as a concomitant condition. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Not related Although information is limited, noting reporter's causality assessment and the nature of the adverse event, it is unlikely for the suspect drug to have a role on hemorrhage based on known drug mechanism of action. Follow-up: No change in assessment.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	134 IU/kg/week, Freq: 3 week, Interval: 1; Subcutaneous	Renal Anaemia (Nephrogenic anaemia)	29-APR-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. The patient had diabetic nephropathy which led to renal failure (first diagnosed on 22-Feb-2012) and was receiving renal dialysis since 10-Jan-2014 with an average of three dialysis per week. The patient had not received any other erythropoietin stimulating agents (ESA) before treatment with Retacrit. The patient had peripheral vascular disease. Race/Ethnicity: Caucasian The patient died on 07-Apr-2014. Cause of death was reported as cerebral haemorrhage. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Peripheral vascular disease (Peripheral vascular disorder);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure); first diagnosed on 22-Feb-2012
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Dialysis (Dialysis); Since 10-Jan-2014

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	13	JAN	1942	73 Years	Male	76.00 kg	22	FEB	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiac arrest [Cardiac arrest]
Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction, fatal cardiac arrest. Epoetin zeta. Serious Hospira-sponsored study report from Greece, received from a physician (ref: Gr-002-0025) which refers to a 73-year-old Caucasian male patient (dry weight: 76 kg;
height: 158 cm). The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 26-FEB-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4Q015R4; Exp.Dt. 01-SEP-2016}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 65.79 IU/k (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 12-JUN-2014 / 22-FEB-2015

19. THERAPY DURATION
#1) 256 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CARVEDILOL (CARVEDILOL) ; Unknown / 26-FEB-2015
#2) FUROSEMIDE (FUROSEMIDE) ; 01-JAN-2005 / 26-FEB-2015
#3) NITROGLYCERIN (GLYCERYL TRINITRATE) ; 01-JAN-2000 / 26-FEB-2015
#4) RANOLAZINE (RANOLAZINE) ; 01-JAN-2014 / 22-FEB-2015
#5) RIVAROXABAN (RIVAROXABAN) ; 01-JAN-2014 / 22-FEB-2015

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2797025

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-MAR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2797025

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had no known drug hypersensitivities and no history of drug dependence. Medical history included ischemic heart failure (ejection fraction was 20-25 %) and bypass surgery in 1986, cardiac pacing, and transient ischemic attack in 2008. The patient had hypertensive nephropathy which led to renal failure (first diagnosed in 2008). The patient was not on dialysis. From 14-Feb-2014 to 10-Jun-2014, the patient received an erythropoietin stimulating agent (ESA), Abseamed (alfa epoetin, 65.79 IU/kg/week, route of administration not reported) for an unknown indication. The patient did not receive Retacrit prior to the study. Concomitant medications included carvedilol (6.25 mg, 3/4 x 2/day; total daily dose: 9.375 mg) for coronary heart disease/AF, furosemide (total daily dose: 500 mg; 1/2 x 2/day) for heart failure, nitroglycerin (total daily dose: 5 mg; once a day) for coronary heart disease, rivaroxaban (total daily dose: 15 mg; once a day) for atrial fibrillation and ranolazine (total daily dose: 375 mg; once a day) for ischemic heart failure (routes of administration were not reported). On 12-Jun-2014, the patient began treatment with Retacrit (epoetin zeta, 65.79 IU/kg/week, one dosage per week, daily dose reported as 18.8 IU/kg/day; subcutaneous, lot number: 4Q015R4, date of expiry: Sep-2016) for renal anaemia. The patient received the last dose of epoetin zeta prior to the events on 17-Feb-2015. On 22-Feb-2015, the patient experienced myocardial infarction also reported as heart attack and cardiac arrest. It was also reported that the patient presented with chest pain and breathlessness. On the same day, the patient was admitted to the hospital because of the adverse events. Treatment for the events was reported as monitoring. No relevant test or laboratory data were available. The suspect drug was discontinued in response to the events on 22-Feb-2015 and the symptoms did not improve at all.
The patient died on 26-Feb-2015. Causes of death were reported as myocardial infarction and cardiac arrest. It was not reported if an autopsy was performed. The reporter's opinion of causality for the events of fatal myocardial infarction and fatal cardiac arrest in relation to Retacrit was unassessable. Risk factors included coronary heart disease, myocardial infarction, atrial fibrillation, peripheral arterial disease (since 1995), hypertension (since 1972), diabetes mellitus type 2 (since 1975), heart failure NYHA stage III, peripheral angiopathy, and was an ex-smoker (stopped smoking in 1986). 27-Mar-2015: Additional information received from the same reporter regarding the lot number and date expiry of Retacrit administered to the patient. Total daily dose of carvedilol was updated to 9.375 mg (previously 9.4 mg). The reporter stated that the patient's previous exposure to other biosimilars was with Abseamed. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Not assessable (reporter causality not assessable) Hospira causality: Not related Though the suspect drug can theoretically increase the risk for thromboembolic events, patient had numerous comorbidities and cardiovascular risk factors which far outweigh the risk from the suspect drug. These factors include more than two decades of diagnosed coronary artery disease and peripheral arterial disease. - N. Gonzales (23 Mar 2015) Follow-up: No change in previous causality assessment. - N. Gonzales (31 Mar 2015)

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4Q015R4; Exp.Dt. 01-SEP-2016}; Regimen #1	65.79 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	12-JUN-2014 / 22-FEB-2015; 256 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient had no known drug hypersensitivities and no history of drug dependence. Medical history included ischemic heart failure (ejection fraction was 20-25 %) and bypass surgery in 1986, cardiac pacing, and transient ischemic attack in 2008. The patient had hypertensive nephropathy which led to renal failure (first diagnosed in 2008). The patient was not on dialysis. From 14-Feb-2014 to 10-Jun-2014, the patient received an erythropoietin stimulating agent (ESA), Abseamed (alfa epoetin, 65.79 IU/kg/week, route of administration not reported) for an unknown indication. The patient did not receive Retacrit prior to the study. Race/Ethnicity: Caucasian The patient died on 26-Feb-2015. Causes of death were reported as myocardial infarction and cardiac arrest. It was not reported if an autopsy was performed. Risk factors included coronary heart disease, myocardial infarction, atrial fibrillation, peripheral arterial disease (since 1995), hypertension (since 1972), diabetes mellitus type 2 (since 1975), heart failure NYHA stage III, peripheral angiopathy, and was an ex-smoker (stopped smoking in 1986).
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	first diagnosed in 2008	
Unknown	Relevant Med History in 1986	Bypass surgery (Vascular graft);
Unknown	Relevant Med History	Cardiac pacemaker insertion (Cardiac pacemaker insertion);
Unknown	Relevant Med History	Ejection fraction low (Ejection fraction decreased);
Unknown	Relevant Med History in 2008	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor - since 1972	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History Risk Factor - since 1972	Hypertension (Hypertension);
Unknown	Relevant Med History	Angiopathy (Angiopathy);
Unknown	Relevant Med History Risk Factor - since 1995	Peripheral arterial disease (Peripheral arterial occlusive disease);
14-FEB-2014 to 10-JUN-2014	Past Drug Event	ABSEAMED (ABSEAMED); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SWEDEN	02	JAN	1928	87 Years	Male	64.00 kg	06	MAR	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Transient ischemic attack [Transient ischaemic attack]
Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction and transient ischemic attack. Epoetin zeta. Serious Hospira-sponsored study report from Sweden, received from an investigator (reference: Sw-018-0008), which refers to an 87-year-old Caucasian male patient
(weight: 64 kg, height: 180 cm).

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 07-JUN-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 400 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 06-MAY-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALFUZOSIN TEVA (ALFUZOSIN HYDROCHLORIDE) Tablet ; Unknown
#2) ALLOPURINOL NYCOMED (ALLOPURINOL) Tablet ; Unknown
#3) BISOPROLOL SANDOZ (BISOPROLOL FUMARATE) Tablet ; Unknown
#4) IMDUR (ISOSORBIDE MONONITRATE) Tablet ; Unknown
#5) INOLAXOL /00561901/ (STERCULIA URENS) ; Unknown
#6) LASIX /00032601/ (FUROSEMIDE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2819992

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
02-SEP-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.
Patient's medical history included hypertensive nephropathy which led to renal failure diagnosed on an unknown day in Mar-2012 and ischemic heart disease. The patient was not on dialysis and was not treated with an erythropoiesisstimulating agent (ESA). The patient was diagnosed with acute subendocardial infarction, cardiac infarction, Type 1, chronic kidney failure, previous cardiac infarction, status post PCI and status post TIA. Concomitant medications included allopurinol 100 mg tablet (Nycomed, 1x1; 1 DF, once a day at 08:00 h) as preventive drug against arthritis, amlodipine Accord 5 mg tablet (1x1; 1 DF, once a day) for high blood pressure, Inolaxol granules also reported as orally administered powder in single-dose sachets or packets (1+0+0+0; 1 single-dose sachet a day, at 08:00 h as needed, to be taken with liquid) which regulates intestinal function, Levaxin 75 mcg tablet (1+0+0+0; 1 DF daily at 08:00 h) for metabolism; alfuzosin Teva prolonged-release tablet 10 mg (1x1; 1 tablet at 20:00 h), bisoprolol Sandoz film-coated tablet 1. 25 mg (1x1; 1 tablet at 08:00 h), Imdur prolonged-release tablet 30 mg (1x1; 1 tablet at 08:00 h), Lasix Retard prolonged-release capsule, hard 30 mg (1x1; 1 capsule at 08:00 h) for unknown indications; all routes of administration were not reported; Terracortril with polymyxin B eye-ear drops (3 drops, 3 times daily in left ear a few days prior to visit, otherwise, as needed) for an unknown indication and Resonium powder for oral/ rectal suspension (1 scoop =15 g, oral, twice a week) to decrease potassium levels. On 06-May-2013, the patient started treatment with Retacrit solution for injection, prefilled syringe 3000 IE/0.9 ml also reported as 3000 U/9 ml (epoetin zeta, lot number unknown, 400 IU/kg/week also reported as 3000 IU/kg every second week, also reported as 1 injection every other week; 14 days schedule, Day 9: 1 dose at 08:00, Day 1-8 and 10-14: none, thereafter repeat schedule; frequency also reported as 1 dose every 14th day, subcutaneous) for renal anaemia also reported as to promote blood formation. On 06-Mar-2015, the patient experienced transient ischemic attack. On the same day, at 1:00pm, the patient was admitted to the hospital because of the suspicion of stroke. It was reported that at 1pm, the patient suddenly felt weakness in his right leg and his leg gave way. He then felt weakness spreading to his left hand and had difficulty speaking. It was also reported that the patient had no strength in his left arm and that the corner of his mouth was still slightly uneven. He had no headache, dizziness or nausea. On 17-Nov-2014 at 8:50 patient's haemoglobin was at 129 g/L (normal values 134-170) while on 06-Mar-2015 at 14:42 , patient's haemoglobin was at 116 g/L, CRP was 5.0 mg/L (normal values: less than 4.0), potassium was 5.8 mmol/L (normal values: 3.2 - 4.6), creatinine was 332 mcmol/L (normal values: 60 - 105), and TNI was 17 ng/L (normal value: less than 35), and patient's blood pressure was 150/75. On an unknown date, neurology showed pupils isocoric and reacting to direct and indirect light, no facial asymmetry, no deviation of the lungs, sensation equal bilaterally, coarse force in the extremities equal, Grasset's test was negative, finger-to-nose manoeuvre normal, normal finger movements, no diadochokinesis, testing the hearing was difficult because of the patient's extremely poor hearing and hearing aid, however, his field of view is normal, reflexes equal bilaterally, Babinski test was negative. It was reported that it was very difficult to rate the patient on Romberg's test given his poor balance in the past and the fact that he uses a Zimmer frame at home. However, the patient manages to stand for short periods of time and keep the balance. No treatment was given in response to the adverse event. Action taken with the suspect drug was not reported. Outcome of the adverse event of transient ischemic attack was recovered on the same day of 06-Mar-2015. On 25-Mar-2015 at 16:00, patient's potassium was 4.4 mmol/L. On 07-Apr-2015 at 08:10, patient's haemoglobin was 118 g/L, CRP was 20 mg/L, potassium was 4.8 mmol/L, creatinine was 322 mcmol/L. On 07-May-2015 at 08:57, patient's haemoglobin was 118 L, potassium 4.8 mmol/L and creatinine was 370 mcmol/L. On 01-Jun-2015, the patient developed ischemic heart disease reported as myocardial infarction. On the same day, the patient was admitted to a hospital because of the event which was considered life threatening. On the same day at 15:50, patient's haemoglobin was 99 g/L, CRP was 8.4 mg/L, potassium was 5.7 mmol/L, creatinine was 387 mcmol/L and TNI was 204 ng/L. The patient arrived with pain in the left axis and arm with no definite ischemic changes on EKG. On the same day at 16:00, EKG showed possible left atrial enlargement and appeared to be suspected pathological and may be limited by ischemic coronary disease/stress, interpreted as NSTEMI. The patient was decided to be on conservative treatment. On an unknown date, the patient underwent an in-house brain CT-scan which showed previously known aneurysm in the rear circulus willisi, as well as widespread white substance changes periventricular, no haemorrhaging. On the same day at 19:05, patient's TNI was 1516 ng/L. On 02-Jun-2015 at 04:00, patient's TNI was 35314 ng/L. On the same day at 07:30, patient's potassium was 5.2 mmol/L and creatinine was 364 mcmol/L. On 03-Jun-2015, fever initiated at 38 degrees. It was reported that the patient was put on Ciaforan 500 mg (dose and route of administration not reported) 3 times due to kidney function. On the same day, lung x-ray carried out, which showed an enlarged heart, but no signs of pneumonia. On the same day at 14:00, CRP was 130 mg/L. On 05-Jun-2015 at 07:30, the patient's haemoglobin was 99 g/L, CRP was 206 mg/L, potassium was 4.5 mmol/L and creatinine was 450 mcmol/L. It was reported that the fever spike and the inflammation markers were determined to be related to the infarction and there was no infection. Antibiotics were ruled out. Due to sharply reduced kidney function with GFR at 11, as well as the anamnesis of previous severe GI-bleeding, Brilique was not considered, Aspirin (Trombyl) and amlodipin were ruled out. It was reported that the patient was refrained from blood thinners due to kidney function and previous GI bleeding. The patient was put on Imdur, Lasix, and Bisoprolol. The patient was discharged on the same day. It was reported that blood pressure on release to home was 110/60 and weight on release to home was 64.6 kilograms. The patient was free of pain for most of the admission period, and appeared healthy. The patient was evaluated with serious kidney failure and dementia development as well as pyelostomy catheter. The patient died on 07-Jun-2015. Cause of death was myocardial infarction. Results of a Post-Mortem examination were not available. The reporter's opinion of causality between the events and the suspect drug was not assessable. Risk factor included hypertension and immobilization.
14-Apr-2015: English translation of Swedish text was received. Stroke was added as an additional event. Dose of Resonium was provided. Frequencies and indications of the concomitant medications were updated. Laboratory and diagnostic

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

tests were provided. Frequency of suspect drug also reported as 1 injection every other week, and indication was also reported as to promote blood formation. Data entry correction was made to remove result of 129g/dl on 17-Nov-2014 on the medical history, and hemoglobin at 116 g/dl as laboratory result. This information has been incorporated in the narrative and corresponding data fields. 15-May-2015: Follow-up information was received from the reporter. The adverse event of stroke was deleted. This information has been incorporated in the narrative and corresponding data fields. 15-Jul-2015: Additional information was received from the reporter. Fatal myocardial infarction was added as adverse event. Life threatening and hospitalization were also added as seriousness criteria. The dose of the suspect drug Retacrit was also reported as 14 days schedule, Day 9: 1 dose at 08:00, Day 1-8 and 10-14: none, thereafter repeat schedule, also reported as 1 dose every 14th day. Patient's weight was updated to 64 kg (previously reported as 65 kg), date of birth day was added. The patient was diagnosed with acute subendocardial infarction, cardiac infarction, Type 1, chronic kidney failure, previous cardiac infarction, status post PCI and status post TIA. Time of administration for the concomitant medications allopurinol, Inolaxol and Levaxin were added. Allopurinol Nordic Drugs was updated to allopurinol Nycomed. Alfuzosin teva, bisoprolol Sandoz, Imdur, Lasix and Terracortril with polymyxin B were added as concomitant medications. Dosage form of Inolaxol was also reported as orally administered powder and frequency was added. Dose of Resonium was updated to 1 scoop=15 g previously reported as 1 scoop=15 mg and route of administration was added. Additional laboratory/diagnostic data of haemoglobin, CRP, potassium, creatinine, TNI, CT-scan, Lung X-ray and EKG were added. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Not assessable Although the suspect drug can theoretically increase the risk of thromboembolic events, cannot provide a definitive assessment without a more detailed medical history including baseline hemoglobin values prior to drug administration. Patient's hypertension and immobilization are also major contributory factors. - N. Gonzales (08 Apr 2015) Follow-up: Overall case causality: Not assessable. No change in assessment for TIA. Stroke with the same causality assessment. While updates are noted, still no information on CV risk factors and baseline values. Follow-up: No change in previous assessment. Follow-up: Causation for the myocardial infarction also cannot be assessed without baseline hemoglobin values as patient had numerous comorbidities as confounding factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Babinski reflex test		
2		Babinski reflex test	Negative, Unknown	
3		Blood creatinine		105 60
4	06-MAR-2015	Blood creatinine	332, MCMOL/L	105 60
5	07-APR-2015	Blood creatinine	332 , MCMOL/L	105 60
6	07-MAY-2015	Blood creatinine	370 ,MCMOL/L	105 60
7	01-JUN-2015	Blood creatinine	387, MCMOL/L	105 60
8	02-JUN-2015	Blood creatinine	364, MCMOL/L	105 60
9	03-JUN-2015	Blood creatinine	450, MCMOL/L	105 60
10	06-MAR-2015	Blood potassium	5.8 mmol/l	4.6 3.2
11	07-APR-2015	Blood potassium	4.8 mmol/l	4.6 3.2
12	07-MAY-2015	Blood potassium	4.8 mmol/l	4.6 3.2
13	01-JUN-2015	Blood potassium	5.7 mmol/l	4.6 3.2
14	02-JUN-2015	Blood potassium	5.2 mmol/l	4.6 3.2
15	05-JUN-2015	Blood potassium	4.5 mmol/l	4.6 3.2

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
16	05-JUN-2015	Blood pressure measurement	110/60, Unknown	
17	06-MAR-2015	C-reactive protein	5.0 mg/l	
18	07-APR-2015	C-reactive protein	20 mg/l	
19	01-JUN-2015	C-reactive protein	8.4 mg/l	
20	03-JUN-2015	C-reactive protein	130 mg/l	
21	05-JUN-2015	C-reactive protein	206 mg/l	
22	03-JUN-2015	Chest X-ray	Enlarged heart but no signs of pneumonia, Unknown	
23		Computerised tomogram	No haemorrhaging, Unknown	
24		Computerised tomogram	White substance changes periventricular,Unknown	
25		Computerised tomogram	Aneurysm in the rear circulus willisi, Unknown	
26	01-JUN-2015	Electrocardiogram	Limited by ischemic coronary disease/stress Unknow	
27	01-JUN-2015	Electrocardiogram	Possible left atrial enlargement, Unknown	
28	01-JUN-2015	Electrocardiogram	NSTEMI, Unknown	
29	01-JUN-2015	Electrocardiogram	Appears to be suspected pathological, Unknown	
30		Glomerular filtration rate	11, Unknown	
31	17-NOV-2014	Haemoglobin	129 g/l	170 134
32	06-MAR-2015	Haemoglobin	116 g/l	170 134
33	07-APR-2015	Haemoglobin	118 g/l	170 134
34	07-MAY-2015	Haemoglobin	118 g/l	170 134
35	05-JUN-2015	Haemoglobin	99 g/l	170 134
36	05-JUN-2015	Haemoglobin	99 g/l	170 134
37		Neurological examination	Negative, Unknown	
38		Neurological examination	Sensation equal bilaterally, Unknown	
39		Neurological examination	No diadochokinesis, Unknown	
40		Neurological examination	Normal finger movements, Unknown	

Mfr. Control Number: 2819992

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
41		Neurological examination	Pupils isocoric and, Unknown	
42		Neurological examination	Finger-to-nose manoeuvre normal, Unknown	
43		Neurological examination	No facial asymmetry, Unknown	
44		Neurological examination	Reacting to direct and indirect light, Unknown	
45		Neurological examination	Coarse force in the extremities equal, Unknown	
46		Neurological examination	Field of view was normal, Unknown	
47		Neurological examination	No deviation of the lungs, Unknown	
48	03-JUN-2015	Pyrexia	38 degrees, Unknown	
49	06-MAR-2015	Troponin I	17 ng/ml	
50	01-JUN-2015	Troponin I	204 ng/ml	
51	01-JUN-2015	Troponin I	1516 ng/ml	
52	02-JUN-2015	Troponin I	35314 ng/ml	
53	05-JUN-2015	Weight	64.6 kg	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	400 IU/kg, 14 days schedule, Day 9; 1 dose at 08:00, Day 1-6 and 10-14 none. thereafter repeat sched; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	06-MAY-2013 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) RESONIUM (SODIUM POLYSTYRENE SULFONATE) ; Unknown

#8) TERRA-CORTRIL POLYMYXIN B (HYDROCORTISONE ACETATE, OXYTETRACYCLINE HYDROCHLORIDE, POLYMYXIN B SULFATE) Ear drops ; Unknown

#9) AMLODIPINE (AMLODIPINE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Tobacco usage and alcohol consumption were not reported. Patient's medical history included hypertensive nephropathy which led to renal failure diagnosed on an unknown day in Mar-2012 and ischemic heart disease. The patient was not on dialysis and was not treated with an erythropoiesis-stimulating agent

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		(ESA). The patient was diagnosed with acute subendocardial infarction, cardiac infarction, Type 1, chronic kidney failure, previous cardiac infarction, status post PCI and status post TIA. Risk factor included hypertension and immobilization. Race/ Ethnicity: Caucasian The patient died on 07-Jun-2015. Cause of death was myocardial infarction. Results of a Post-Mortem examination were not available.
Unknown to Ongoing	Relevant Med History	Acute myocardial infarction, subendocardial infarction (Acute myocardial infarction);
Unknown to Ongoing	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown to Ongoing	Relevant Med History	Kidney failure chronic (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Dementia (Dementia);
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History Diagnosed on an unknown date in Mar-2012	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Percutaneous coronary intervention (Percutaneous coronary intervention);
Unknown	Relevant Med History	TIA (Transient ischaemic attack);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Immobile (Immobile);
Unknown	Relevant Med History	Ureteropyelostomy (Ureteropyelostomy);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	11	NOV	1939	74 Years	Male	88.00 kg	01	MAY	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (reference: Ge-454-0018), which refers to a 74-year-old Caucasian male patient (dry weight: 88 kg also
reported as 84 kg, height: 182 cm). The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 45 IU/kg, Freq: 1 week, Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 18-JUN-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL HEUMANN (ALLOPURINOL) Tablet ; Unknown
#2) BERODUAL (FENOTEROL HYDROBROMIDE, IPRATROPIUM BROMIDE) ; Unknown
#3) DIGITOXIN (DIGITOXIN) Tablet ; Unknown
#4) FENISTIL (DIMETINDENE MALEATE) ; Unknown
#5) FERINJECT (FERRIC CARBOXYMALTOSE) Solution for injection i
#6) GALVUS (VILDAGLIPTIN) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2817079

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
15-JAN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Patient’s medical history included hypertensive nephropathy which led to renal failure diagnosed on 18-Jun-2013 and transient ischemic attack. The patient was not on dialysis, was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit, and has not received Retacrit prior to the study. Concomitant medications included ‘Sweden’ 250 mg tablet (sodium chloride, 1-1-1-0) for hyponatremia, Fenistil 24 hour retard capsule (0-0-0-1) against itching, Galvus 50 mg tablet (1-0-0-0) new against sugar; Ramipril Hexal 5 mg/25 mg tablet (1-0-0-0), Torasemid AL 200 mg tablet (1/4-1/4-0-0; dose reported as increased), digitoxin 0.07 mg tablet (1-0-0-0), pantoprazole TAD 40 mg enteric coated tablet (1-0-2-0), simvastatin Actavis 40 mg film-coated tablet (0-0-1/2-0), allopurinol 100 Heumann tablet (1-0-0-0), Viani 50 mcg/250 mcg diskus powder for inhalation (1-0-1-0), Berodual N metered dose inhaler (2-0-2-0), Spiriva 18 mcg refill capsules (1-0-0-0), Marcumar tablet (dose not reported), Levemir Flexpen 100 units/ml in a pre-filled syringe (0-0-0-10 IE), (routes of administration not reported); and Ferinject 50 mg iron/ml Inj./Inf. In a pre-filled syringe (1-0-0-0 in 10 ml of iron infusion) in 0.9% NaCl (250 ml, for over an hour), all given for unknown indications. On 11-Jun-2013, Hb was 10.2 g/dl and Hkt was 35.2 % (normal values not reported). On 18-Jun-2013, the patient started treatment with Retacrit (epoetin zeta, 45 IU/kg/week, 1 dosage/week, dose also reported as 1-0-0-0, subcutaneous, 4000 IU/0.4 ml Inj. in a pre-filled syringe, lot number unknown) for renal anaemia. Laboratory tests on the following dates showed the following results: on 17-Sep-2013, Hb was 11.8 g/dl and Hkt was 39.2 %; on 16-Dec-2013, Hb was 12.2 g/dl and Hkt was 38.8 %; and on 20-Mar-2014, Hb was 11.9 g/dl and Hkt was 38.4 %. On an unknown day in May-2014, the patient developed myocardial infarction. Treatment for the adverse event and action taken with the suspect drug were not reported. On an unknown date, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal myocardial infarction in relation to epoetin zeta was not reported. Risk factors included COPD since 2000, ischemic heart disease in 1990 where patient had ACVB operation in 2005, coronary heart disease, atrial fibrillation since 2009, hypertension since 1990, heart failure NYHA stage III, and type 2 diabetes mellitus since 2000 with diabetic vascular complications. 06-Apr-2015: Additional information was received from the same reporter. Patient's weight was also reported as 84 kg. Concomitant medications, formulation of Retacrit and laboratory tests were provided. Dose of Retacrit was also reported as 1-0-0-0. Transient ischemic attack was added as medical history. Ischemic heart disease where patient had ACVB operation, and COPD were added as risk factors. Atrial fibrillation, hypertension and diabetes were reported to be in occurrence since 2009, 1990 and 2000, respectively. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product: lot number and date of expiry, and previous exposure of patient to other biosimilars. 15-Apr-2015: English translation of German text was received. Schweden tablet was changed to ‘Sweden’ tablet and formulation strength was changed to 250 mg (previously reported as 0.25. Dosage form of Ferinject and active ingredient of Schweden tablet were provided. This information has been incorporated in the narrative and corresponding data fields. Data entry correction was also made to reflect dosage form of ‘Sweden’ tablet in the data field.

Follow Up (IRD:30-MAR-2015 PRD: 30-MAR-2015)

Fatal myocardial infarction. Epoetin zeta. Hospira-sponsored study report from an investigator (reference: Ge-454-0018), which refers to a patient. The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Patient’s medical history included hypertensive nephropathy which led to renal failure diagnosed on 18-Jun-2013 and transient ischemic attack. The patient was not on dialysis, was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit, and has not received Retacrit prior to the study. Concomitant medications included ‘Sweden’ 250 mg tablet, Fenistil 24 hour retard capsule, Galvus 50 mg tablet, Ramipril Hexal 5 mg/25 mg tablet, Torasemid AL 200 mg tablet, digitoxin 0.07 mg tablet, pantoprazole TAD 40 mg enteric coated tablet, simvastatin Actavis 40 mg film-coated tablet, allopurinol 100 Heumann tablet, Viani 50 mcg/250 mcg diskus powder for inhalation, Berodual N metered dose inhaler, Spiriva 18 mcg refill capsules, Marcumar tablet, Levemir Flexpen 100 units/ml in a pre-filled syringe, and Ferinject 50 mg iron/ml Inj./Inf. In a pre-filled syringe in 0.9% NaCl. On 11-Jun-2013, Hb was 10.2 g/dl and Hkt was 35.2 % (normal values not reported). On 18-Jun-2013, the patient started treatment with Retacrit (epoetin zeta, 45 IU/kg/week, 1 dosage/week, dose also reported as 1-0-0-0, subcutaneous, 4000 IU/0.4 ml Inj. in a pre-filled syringe, lot number unknown) for renal anaemia. Laboratory tests on the following dates showed the following results: on 17-Sep-2013, Hb was 11.8 g/dl and Hkt was 39.2 %; on 16-Dec-2013, Hb was 12.2 g/dl and Hkt was 38.8 %; and on 20-Mar-2014, Hb was 11.9 g/dl and Hkt was 38.4 %. On an unknown day in May-2014, the patient developed myocardial infarction. Treatment for the adverse event and action taken with the suspect drug were not reported. On 11-May-2014, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal myocardial infarction in relation to epoetin zeta was not reported. Risk factors included COPD since 2000, ischemic heart disease in 1990 where patient had ACVB operation in 2005, coronary heart disease, atrial fibrillation since 2009, hypertension since 1990, heart failure NYHA stage III, and type 2 diabetes mellitus since 2000 with diabetic vascular complications. 06-Apr-2015: Additional information was received from the same reporter. Patient's weight was also reported as 84 kg. Concomitant medications, formulation of Retacrit and laboratory tests were provided. Dose of Retacrit was also reported as 1-0-0-0. Transient ischemic attack was added as medical history. Ischemic heart disease where patient had ACVB operation, and COPD were added as risk factors. Atrial fibrillation, hypertension and diabetes were reported to be in occurrence since 2009, 1990 and 2000, respectively. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product: lot number and date of expiry, and previous exposure of patient to other biosimilars. 15-Apr-2015: English translation of German text was received. Schweden tablet was changed to ‘Sweden’ tablet and formulation strength was changed to 250 mg (previously reported

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

as 0.25. Dosage form of Ferinject and active ingredient of Schweden tablet were provided. This information has been incorporated in the narrative and corresponding data fields. Data entry correction was also made to reflect dosage form of 'Sweden' tablet in the data field. 15-Jan-2016: Additional information was received from the same reporter. Death date was provided. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Althoug the suspect drug can theoretically increase the risk of thrombosis, cannot provide causation of event due to limited information regarding timeline, medical history, concomitant medications and other objective clinical event details. - N. Gonzales (07 Apr 2015) Follow-up: New information noted. Company causality changed to not related given the new information and the preexistent ischemic heart disease in the medical history. Although the suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration, the patient's numerous cardiovascular risk factor outweigh this potential risk. Patient's hemoglobin was also not significantly increased compared to 9 months prior. - N. Gonzales (14 Apr 2015) Follow-up: No change in previous causality assessment. - N. Gonzales (23 Apr 2015)
Follow Up (IRD:30-MAR-2015 PRD: 30-MAR-2015)
Overall case causality: Possible Hospira causality: Not assessable Althoug the suspect drug can theoretically increase the risk of thrombosis, cannot provide causation of event due to limited information regarding timeline, medical history, concomitant medications and other objective clinical event details. Follow-up: New information noted. Company causality changed to not related given the new information and the preexistent ischemic heart disease in the medical history. Although the suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration, the patient's numerous cardiovascular risk factor outweigh this potential risk. Patient's hemoglobin was also not significantly increased compared to 9 months prior. Follow-up: No change in previous causality assessment. Follow-up: No change in assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-JUN-2013	Haematocrit	35.2 %	
2	17-SEP-2013	Haematocrit	39.2 %	
3	16-DEC-2013	Haematocrit	38.8 %	
4	20-MAR-2014	Haematocrit	38.4 %	
5	11-JUN-2013	Haemoglobin	10.2 g/dl	
6	17-SEP-2013	Haemoglobin	11.8 g/dl	
7	16-DEC-2013	Haemoglobin	12.2 g/dl	
8	20-MAR-2014	Haemoglobin	11.9 g/dl	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#5) FERINJECT (FERRIC CARBOXYMALTOSE) Solution for injection in pre-filled syringe ; Unknown

#7) LEVEMIR (INSULIN DETEMIR) Solution for injection in pre-filled syringe ; Unknown

#8) MARCUMAR (PHENPROCOUMON) Tablet ; Unknown

#9) PANTOPRAZOL TAD (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

#10) RAMIPRIL HEXAL (RAMIPRIL) Tablet ; Unknown

#11) SIMVASTATIN ACTAVIS (SIMVASTATIN) Tablet ; Unknown

#12) SPIRIVA (TIOTROPIUM BROMIDE) ; Unknown

#13) TORASEMID AL (TORASEMIDE) Tablet ; Unknown

Mfr. Control Number: 2817079

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#14) VIANI (FLUTICASONE PROPIONATE, SALMETEROL XINAFOATE) Inhalation powder ; Unknown

#15) SODIUM CHLORIDE (SODIUM CHLORIDE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. Patient's medical history included hypertensive nephropathy which led to renal failure diagnosed on 18-Jun-2013 and transient ischemic attack. The patient was not on dialysis, was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit, and has not received Retacrit prior to the study. Risk factors included COPD since 2000, ischemic heart disease in 1990 where patient had ACVB operation in 2005, coronary heart disease, atrial fibrillation since 2009, hypertension since 1990, heart failure NYHA stage III, and type 2 diabetes mellitus since 2000 with diabetic vascular complications. Race/ Ethnicity: Caucasian On an unknown date, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History 2005	Aortocoronary bypass (Coronary artery bypass);
Unknown	Relevant Med History Risk Factor	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History Risk Factor-2000	COPD (Chronic obstructive pulmonary disease);
Unknown	Relevant Med History Risk Factor	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Risk Factor	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor	Diabetic vascular disorder (Diabetic vascular disorder);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	18	SEP	1960	54 Years	Male	67.00 kg	13	FEB	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Suspected acute myocardial infarction [Acute myocardial infarction]

Case Description: Fatal suspected acute myocardial infarction. Epoetin zeta. Serious Hospira sponsored clinical study report from Germany received from an investigator (reference: Ge-109-0003), which refers to a 54-year-old Caucasian male (dry weight:
67 kg, height: 181 cm). Medical history included diabetic nephropathy which led to renal failure diagnosed on 25-May-2007. The patient was on hemodialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 13-FEB-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 67 IU/kg/w (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 02-DEC-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) LANTUS (INSULIN GLARGINE) ; Unknown
#2) NOVORAPID (INSULIN ASPART) ; Unknown
#3) PANTOPRAZOL BIOMO (PANTOPRAZOLE SODIUM SESQUIHYDRAT
#4) SIMVA (SIMVASTATIN) ; Unknown
#5) TOREM /01036501/ (TORASEMIDE) Tablet ; Unknown
#6) CARVEDILOL (CARVEDILOL) Tablet ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2820900

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-APR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

treatment with Retacrit and had not received Retacrit prior to the study. Concomitant medications included Lantus 100 U/ml cartridge cylinder ampoule (20 IU in the evening), Torem 10 tablet (3 DF, in the morning), Novorapid Penfill. 100 U/ML (14 units in the morning and evening, 10 units around lunchtime, I.U. by blood sugar and plan), pantoprazole Biomo 40 mg tablet (1 DF in the morning and in the evening), carvedilol AL 12.5 mg tablet (0.5 DF in the morning and in the evening), and Simva Hennig 20 mg film coated tablet (1 DF, in the evening), routes of administration not reported, all given for unknown indications. The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. On 02-Dec-2013, the patient started treatment with Retacrit (epoetin zeta, 67 IU/kg/week, 1 dosage per week, subcutaneous; lot number not reported) for renal anaemia. On 19-Jan-2015, haemoglobin was at 9.7 g/dl (normal range: 13.3-17.7), hematocrit was 32% (normal range: 40.0-52.0), cholesterol HDL was 48.2 mg/dl (normal range >50), cholesterol LDL was 74.3 (normal range: <150), triglyceride was 71.3 mg/dl (normal range: 0-200), PTT was 34 sec (normal range: 26.0-42.0), and INR-Wert. kA was 1.1 INR (normal range: 1.00-1.24). On 09-Feb-2015, haemoglobin was at 9.8 g/dl and hematocrit was 30%. On 13-Feb-2015, the patient experienced suspected acute myocardial infarction described as an acute pain in chest and left arm during hemodialysis. The patient was then admitted to hospital for primary care. It was reported that the date of last dose of epoetin zeta prior to the adverse event was on the same day of 13-Feb-2015. Treatment for the event and action taken with the suspect drug were not reported. On 13-Feb-2015, the patient died. Cause of death was suspected acute myocardial infarction. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal suspected acute myocardial infarction in relation to epoetin zeta was reported as unlikely and not related. Risk factors included immobilization due to amputation of right leg on 01-Jan-2014, ischemic heart disease in 2012, peripheral arterial disease since 2012, hyperlipidaemia, hypertension, diabetes mellitus type 1 since 1970 with vascular complications, and heart failure NYHA stage II. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: lot number, date of expiry, and previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Probably Not Hospira causality: Not related Although the suspect drug can theoretically increase the risk of thromboembolic events, the patient's preexistent cardiovascular comorbities and risk factors (ischemic heart disease since 2012, hyperlipdemia, diabetes, hypertension and immobilization) far outweigh the potential risk from the suspect drug. Patient's hemoglobin was also still below normal values at the time of the event. - N. Gonzales (09 Apr 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	19-JAN-2015	Activated partial thromboplastin time	34 seconds	42.0 26.0
2	19-JAN-2015	Blood triglycerides	71.3 mg/dl	200 0
3	19-JAN-2015	Haematocrit	32 %	52.0 40.0
4	09-FEB-2015	Haematocrit	30 %	52.0 40.0
5	19-JAN-2015	Haemoglobin	9.7 g/dl	17.7 13.3
6	09-FEB-2015	Haemoglobin	9.8 g/dl	17.7 13.3
7	19-JAN-2015	High density lipoprotein	74.3 mg/dl	
8	19-JAN-2015	High density lipoprotein	48.2 mg/dl	
9	19-JAN-2015	International normalised ratio	1.1 INR, Unknown	1.24 1.00

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution	67 IU/kg/week, Freq: 1	Renal anaemia (Nephrogenic	02-DEC-2013 /

Mfr. Control Number: 2820900

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
for injection; Regimen #1	week, Interval: 1; Subcutaneous	anaemia)	Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) PANTOPRAZOL BIOMO (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to renal failure diagnosed on 25-May-2007. The patient was on hemodialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit and had not received Retacrit prior to the study. Risk factors included immobilization due to amputation of right leg on 01-Jan-2014, ischemic heart disease in 2012, peripheral arterial disease since 2012, hyperlipidaemia, hypertension, diabetes mellitus type 1 since 1970 with vascular complications, and heart failure NYHA stage II. Race/Ethnicity: Caucasian On 13-Feb-2015, the patient died. Cause of death was suspected acute myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History 01-Jan-2014	Leg amputation (Leg amputation);
Unknown	Relevant Med History Since 1970	Type I diabetes mellitus with peripheral circulatory disorders (Diabetic vascular disorder);
Unknown	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Immobilization prolonged (Immobilisation prolonged);
Unknown	Relevant Med History 2012	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Since 2012	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	22	OCT	1962	Unk	Female	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiogenic shock [Cardiogenic shock]
Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction and fatal cardiogenic shock. Epoetin zeta. Serious Hospira-sponsored clinical study report from Bulgaria, received from an investigator (reference: Bg-014-0003), which refers to a Caucasian female patient (dry
weight: 90 kg, height: 162 cm; age not reported).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 09-APR-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 66 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 05-NOV-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2939556

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-JUL-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2939556

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-sponosored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included diabetic nephropathy which led to renal failure diagnosed in 2010. The patient was not on dialysis. The patient was not treated with an ESA before treatment with Retacrit. Concomitant medications were not reported. On 05-Nov-2013, the patient started treatment with epoetin zeta (Retacrit; 66 IU/kg/week, 2 dosages/week, subcutaneous; lot number not reported) for renal anaemia. The patient was enrolled in the study on 23-Oct-2013. On an unknown date, the patient experienced myocardial infarction and cardiogenic shock. Investigations including examinations, laboratory, diagnostic data; treatment for the adverse events, and action taken with the suspect drug were not reported. On 09-Apr-2015, the patient died. Cause of death was myocardial infarction and cardiogenic shock. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event and epoetin zeta was not reported. Risk factors included hypertension and diabetes type I with vascular complications. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: lot number, date of expiry, and previous exposure of patient to other biosimilars besides epoetin zeta.

Case Comment: Overall case causality: Possible (reporter causality not provided) Hospira causality: Not assessable Although the suspect drug can theoretically increase the risk of thromboembolic events, cannot provide a definite causation without firm timeline, objective clinical event details and a more detailed medical history.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	66 IU/kg, Freq: 2 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	05-NOV-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to renal failure diagnosed in 2010. The patient was not on dialysis. The patient was not treated with an ESA before treatment with Retacrit. Risk factors included hypertension and diabetes type I with vascular complications. On 09-Apr-2015, the patient died. Cause of death was myocardial infarction and cardiogenic shock. It was not reported if an autopsy was performed. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Type I diabetes mellitus with peripheral circulatory disorders (Diabetic vascular disorder);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GREECE	26	MAR	1932	83 Years	Female	58.00 kg	24	JUL	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Stroke [Cerebrovascular accident]

Case Description: Fatal stroke. Epoetin zeta. Serious Hospira-sponsored study report from Greece, received from an investigator (ref: Gr-052-0006), which refers to an 83-year-old Caucasian female patient (dry weight: 58 kg, height: 150 cm). The patient
was enrolled in a Hospira sponsored study entitled Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had no known drug

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 31-JUL-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S027S4}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 310/kg/week (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 07-JAN-2013 / 24-JUL-2015

19. THERAPY DURATION
#1) 929 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FOSRENOL (LANTHANUM CARBONATE) ; 01-JUL-2014 / 01-JAN-2015
#2) INTELECTA (LEVOCARNITINE) ; 01-JUL-2014 / 01-JUL-2015

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2965870

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

hypersensitivities, had no history of drug dependence, was not obese, and not a smoker. Medical history included ischemic heart disease and diabetic nephropathy which led to renal failure diagnosed in 18-Sep-2011. The patient was on hemodialysis since 14-Nov-2012 with an average frequency of 3 per week. The patient was not pregnant at the time of treatment. The patient was previously treated with an erythropoiesis-stimulating agent (ESA) darbepoetin alfa (Aranesp; 30/week, route of administration not reported) with first treatment on 18-Sep-2011 prior to treatment with Retacrit. It was reported that the patient did not experience any thromboembolic event during treatment with Aranesp. Concomitant medications included Monoter (1; 2 per week, intravenous) for renal anemia, Intelecta (1; 3 per week, intravenous) for renal disease, and Fosrenol (1; 3 per day, oral) (dosage units not reported) for hyperphosphatemia. On 07-Jan-2013, the patient started to receive epoetin zeta (Retacrit; lot number: 4S027S4, 310/kg/week, 3 per week, subcutaneous, strength: 6000) for renal anemia. On 17-Feb-2014, the patient was enrolled into the study. On 24-Jul-2015, the patient experienced stroke. Laboratory tests included haemoglobin of 6.6 g/dL and 9.3 g/dL (normal values not reported). It was reported that the dosage of the suspect drug was reduced in response to the adverse event but the symptoms did not improve at all. Therapy end date of the suspect drug was on the same day of 24-Jul-2015. It was reported that the patient was admitted to the hospital from 24-Jul-2015 to 31-Jul-2015 because of the adverse event. The patient died on 31-Jul-2015. Cause of death was stroke. It was unknown if autopsy was performed. The reporter's opinion of causality between the event and the suspect drug was unlikely. Risk factors included coronary heart disease, myocardial infarction, hypertension, and type 2 diabetes with vascular complications. 02-Sep-2015: Additional information was received from the investigator. Patient age was provided; patient weight and height were updated to 58 kg and 150 cm, respectively (previously 61 kg and 151 cm). Medical history ischemic heart disease, history of the patient's drug hypersensitivities and drug dependence; obesity and smoking were provided. Concomitant medications and laboratory tests were also added. Dose and frequency of Retacrit were updated to 310/kg/week and 3/week, respectively (previously 131 IU/kg/week and 2 dosage/week); and therapy end date was provided. Event onset date and dechallenge details were also provided. Hospitalization and life-threatening were added as seriousness criteria. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and previous exposure of patient to other biosimilars. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Although the suspect drug can theoretically increase the risk of thromboembolic events such as stroke, cannot provide definite causation without firm timeline between drug administration and onset of adverse event. Follow-up: Overall case causality: Related Possible contributory effect of the suspect drug - as it does increase the risk of thromboembolic events, but consider also other pre-existing and predisposing CV risk factors (CHD, MI, HPN and DM).

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	9.3 g/dl	
2		Haemoglobin	6.6 g/dl	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S027S4}; Regimen #1	310/kg/week, Freq: 3 week, Interval: 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	07-JAN-2013 / 24-JUL-2015; 929 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption was not reported. The patient had no known drug hypersensitivities, had no history of drug dependence, was not obese, and not a smoker. Medical history included diabetic nephropathy which led to renal failure diagnosed in 18-Sep-2011. The patient was on hemodialysis since 14-Nov-2012 with an average frequency of 3 per week. The patient was not pregnant at the time of treatment. The patient was previously treated with an erythropoiesis-stimulating agent (ESA) darbepoetin alfa (Aranesp; 30/week, route of administration not reported) with first treatment on 18-Sep-2011 prior to treatment with Retacrit. It was reported that the patient did not experience any thromboembolic event during treatment with Aranesp. Risk factors included

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		coronary heart disease, myocardial infarction, hypertension, and type 2 diabetes with vascular complications. Race / Ethnicity: Caucasian The patient died on 31-Jul-2015. Cause of death was stroke. It was not reported if autopsy was performed.
Unknown to Ongoing	Relevant Med History Diagnosed 18-Spe-2011	Renal failure (Renal failure);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History 3 dialysis per week, since 14-Nov-2012	Hemodialysis (Haemodialysis);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);
Unknown	Past Drug Event	DARBEPOETIN ALFA (DARBEPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	02	FEB	1926	89 Years	Male	62.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Acute myocardial infarction]

Case Description: Fatal acute infarct myocardium. Epoetin zeta. Hospira-sponsored study report, received from an investigator (reference: ES-024-0025), which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post Authorisation
Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history included nephroangiosclerosis which led to renal failure diagnosed on 03-Jan-2013. The

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 100 IU/Kg/ weekUNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 09-JAN-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DIGOXINA (DIGOXIN) ; 30-OCT-2014 / Unknown
#2) ENOXAPARINA (ENOXAPARIN SODIUM) ; 01-JAN-2015 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Nephroangiosclerosis (Nephroangiosclerosis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2999144

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-SEP-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2999144

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications included digoxina and enoxaparina. On 09-Jan-2013, the patient began treatment with Retacrit (epoetin zeta; lot number unknown, 100 IU/kg/week, 1 dosage/week, subcutaneous) for renal anaemia. On an unknown date, the patient developed acute infarct myocardium. On an unknown date, RBC was 4.3x10^12/L (reference value: 4-5.1), hemoglobin was 13.2 g/dl (reference value: 13-18), hematocrit was 41% (reference value: 38-52) and platelets were 192x10^9/L (reference value: 130-400). Treatment for the adverse event and action taken with suspect drug were not reported. On 21-Apr-2015, the patient died. Cause of death was acute infarct myocardium. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event and the suspect drug was not related. Risk factors included hypertension, ischemic heart disease, transient cerebral ischemic attack and smoking (ex-smoker). The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 18-Sep-2015: Additional information was received from the same reporter. Laboratory tests were provided. These information has been incorporated in the narrative and corresponding data field.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without a firm timeline, clinical course, objective clinical event details (including pertinent laboratory test results and post-moretem findings, if any) and medical history. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	41 %	52 38
2		Haemoglobin	13.2 g/dl	18 13
3		Platelet count	192 x10 9/l	400 130
4		Red blood cell count	4.3 x10 12/l	5.1 4

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. Medical history included nephroangiosclerosis which led to renal failure diagnosed on 03-Jan-2013. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Risk factors included hypertension, ischemic heart disease, transient cerebral ischemic attack and smoking (ex-smoker). On 21-Apr-2015, the patient died. Cause of death was myocardial infarction. It was not reported if an autopsy was performed.
Unknown	Relevant Med History Risk Factor	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Risk Factor	Transient ischemic attack (Transient ischaemic attack);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GREECE	21	DEC	1935	80 Years	Male	76.00 kg	05	NOV	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Stroke [Cerebrovascular accident]

Case Description: Fatal Stroke. Epoetin zeta. Hospira sponsored study report received from an Investigator, which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit
(epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient has no known drug hypersensitivity and no history of drug dependence. Medical history included renal failure since 2005, on dialysis since 16 Jan

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 05-NOV-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) *NO SUBJECT DRUG (NO SUBJECT DRUG) Unknown {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 28.49 IU/kg/week,3 dosages per week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-APR-2015 / 05-NOV-2015

19. THERAPY DURATION
#1) 219 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATORVASTATIN (ATORVASTATIN) ; Unknown / 05-NOV-2015
#2) CARVEDILOL (CARVEDILOL) ; Unknown / 04-NOV-2015
#3) FUROSEMIDE (FUROSEMIDE) ; Unknown / 05-NOV-2015
#4) IRON SUCROSE (SACCHARATED IRON OXIDE) ; 01-JAN-2015 / 05-NOV-2015
#5) LEVOCARNITIN (LEVOCARNITINE HYDROCHLORIDE) ; 01-JAN-2015 / 05-NOV-2015
#6) OMEPRAZOLE (OMEPRAZOLE) ; Unknown / 05-NOV-2015

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Type II diabetes mellitus (Type 2 diabetes mellitus)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3073610

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-NOV-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

2015, diabetes type II, lung cancer in 1988 which was resolved, hyperlipidemia, hypertension, gastritis and paraproteinemia. It was reported that the patient was previously exposesd to Aranesp. Concomitant medications included iron sucrose, levocarnitine, vit B1 B6 B12, omeprazole, carvedilol, vidagliptin, atorvastatin, Sevelamer, spironolactone and furosemide. On April 2015, the patient started to receive epoetin zeta (Retacrit, 28.49 IU/kg/day, subcutaneous; lot number not reported) for renal anemia. On an unknown date, it was reported that the patient was hospitalized due to high leucocytes and CRP. On 24-Sep-2015, laboratory data of the patient included white blood cell count of 11.2 thousand/mm^3 (normal values: 4.6-10.2), neutrophil count of 72.8 % (normal values: 42-75), lymphocyte count of 13.8 % (normal values: 20.5-50), monocyte count of 13.4 % (normal values: 2-12), red blood cell count of 3.65 m/mm^3 (normal values: 4.7-6.0), hemoglobin of 10.7 gr/dl (normal values: 13.5-18.0), hematocrit of 35.1 % (normal values: 42-52), mean corpuscular volume of 96.2 fl (normal values: 78-100), mean corpuscular hemoglobin of 29.3 Pg (normal values: 27-31), mean corpuscular hemoglobin concentration of 30.5 gr/dl (normal values: 32-36), RBC distribution width of 14.9 % (normal values: 11.5-14.0), platelet count of 287 thousand/mcL (normal values: 140-440), mean platelet volume of 9.9 fl (normal values: 7.5-11.5), platelet large cell ratio of 24.5 % (normal values:6-30) and platelet distribution width of 10.6 % (normal values: 9-17). On 05 Nov 2015 during the hospitalization, the patient died. Cause of death was stroke. It was not reported if an autopsy was performed or not. The reporter's opinion of causality between the event and suspect drug was unassessable. 18-Nov-2015: English translation of the Greek text was received. Laboratory tests on 24 Sep 2015 were added. This information has been incorporated in the narrative and corresponding data field.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Cannot provide event causation without a firm timeline, clinical course and further objective clinical event details (including post-mortem findins and other pertinent test results). Follow up: No change in previous causality assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		C-reactive protein	High Unknown	
2	24-SEP-2015	Haematocrit	35.1 %	52 42
3	24-SEP-2015	Haemoglobin	10.7 g/dl	18.0 13.5
4	24-SEP-2015	Lymphocyte count	13.8 %	50 20.5
5	24-SEP-2015	Mean cell haemoglobin	29.3 pg	31 27
6	24-SEP-2015	Mean cell haemoglobin concentration	30.5 g/dl	36 32
7	24-SEP-2015	Mean cell volume	96.2 FL	100 78
8	24-SEP-2015	Mean platelet volume	9.9 FL	11.5 7.5
9	24-SEP-2015	Monocyte count	13.4 %	12 2
10	24-SEP-2015	Neutrophil count	72.8 %	75 42
11	24-SEP-2015	Platelet count	287 thousand/mcL Unknown	440 140
12	24-SEP-2015	Platelet distribution width	10.6 %	17 9
13	24-SEP-2015	Platelet-large cell ratio	24.5 %	30 6
14	24-SEP-2015	Red blood cell count	3.65 m/mm^3 Unknown	6.0 4.7
15	24-SEP-2015	Red cell distribution width	14.9 %	14.0 11.5
16		White blood cell count	High Unknown	

Mfr. Control Number: 3073610

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
17	24-SEP-2015	White blood cell count	11.2 thousand/mm^3 Unknown	10.2 4.6

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) SEVELAMER (SEVELAMER) ; Unknown / 05-NOV-2015

#8) SPIRONOLACTONE (SPIRONOLACTONE) ; Unknown / 05-NOV-2015

#9) VILDAGLIPTIN (VILDAGLIPTIN) ; Unknown / 05-NOV-2015

#10) VITAMIN B1+B6+B12 (CYANOCOBALAMIN, PYRIDOXINE HYDROCHLORIDE, THIAMINE HYDROCHLORIDE) ; 01-JAN-2015 / 05-NOV-2015

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient has no known drug hypersensitivity and no history of drug dependence. Medical history included renal failure since 2005, on dialysis since 16 Jan 2015, diabetes type II, lung cancer in 1988 which was resolved, hyperlipidemia, hypertension, gastritis and paraproteinemia. It was reported that the patient was previously exposesd to Aranesp. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Gastritis (Gastritis);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Paraproteinemia (Paraproteinaemia);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Lung cancer (Lung neoplasm malignant);
Unknown	Relevant Med History Concurrent procedure	Dialysis (Dialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	01	NOV	1931	82 Years	Male	82.00 kg	03	JUN	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Heart failure [Cardiac failure]
Thromboembolic events [Embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This case has been migrated from another database into the current safety

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 03-JUL-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 73.7 IU, F (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 07-AUG-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN (INSULIN) ; Unknown
#2) CARVEPEN (CARVEDILOL) ; Unknown
#3) LIPITOR (ATORVASTATIN CALCIUM) ; Unknown
#4) SALOSPIR (ACETYLSALICYLIC ACID) ; Unknown
#5) RENITEC /00574902/ (ENALAPRIL MALEATE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Vascular disorder NOS (Angiopathy)
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3084735

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-MAY-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

database for processing follow-up information. As a consequence of this migration, the follow-up CIOMS I or MedWatch report may indicate in the appropriate field that it is an initial report.

The 82-year-old male patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), the report was received from an investigator (ref: Gr-051-0024), which refers to the patient (subject no: 0510024), administered subcutaneously for the treatment of renal anaemia. On 07Aug2012, the patient started to receive treatment of epoetin (Retacrit; lot number unknown, 73.7 IU/kg, per week, subcutaneous) for renal anaemia. The patient had not received Retacrit prior to the study. Epoetin Zeta was administered weekly. Mean dose of epoetin zeta applied within the period of 3 months prior to the event was 5000IU and mean dose of hemoglobin was 10.2 g/dl. The patient was not exposed to any other erythropoietin stimulating agent (ESA). The patient had relevant medical history included vascular anomalies that constitute a risk factor for thromboembolic events, ongoing hyperlipidemia, ongoing ischaemic heart disease, ongoing transient ischaemic attack, ongoing peripheral arterial disease, diabetes mellitus type II from 2006 and ongoing and ongoing hypertension. Concomitant medications included insulin for diabetes mellitus type II, carvedilol (CARVEPEN) at 6.25 (no units provided), 1/2x2 for hypertension, atorvastatin (LIPITOR) at 20 (no units provided), 1x1 for hyperlipidemia, acetylsalicylic acid (SALOSPIR) at 100 (no units provided), 1x1 for peripheral arterial disease and Enalapril (RENITEC) at 20 (no units provided), 1x1 for hypertension. On 20Aug2013, the patient was enrolled to the study and the informed consent was signed. On 03JUN2014, the patient experienced heart failure. On 03Jun2014, during an unscheduled visit, the patient experienced thromboembolic events. There was no blood sample retained during the visit and at the end of the study. Treatment for the adverse events was not reported. On an unspecified date the patient underwent laboratory examinations that showed: haemoglobin 10.2 g/dl, haematocrit 30.9%, red blood cells 31800, leukocytes 6500. The patient was not admitted to the hospital as a result of the events. The patient was withdrawn from the study on 03Jul2014 and had not completed the study due to death. The patient died on 03Jul2014. Cause of death was heart failure/thromboembolic event. It was unknown if an autopsy was performed. The Investigator's opinion of causality between the events and the study drug was not related. 10Mar2016: Additional information was received from the same reporter. Thromboembolic events was added as adverse event. No blood sample was also retained during the visit. This information has been incorporated in the narrative and in the corresponding data fields.

Follow-up (19Jan2018): New information received from a contactable physician includes cause of death and causality assessment.

Follow-up (25Jan2018). New information received from a contactable physician for protocol EPOE-09-11, subject ID 0510024 upon response to the DCA for Thromboembolic events includes patient age, medical history, lab data, updated Concomitant medications.

Follow-up attempts completed. No further information is expected.

Follow-up (17May2018): New information received from the physician includes: the subject ID is 0510024 and patient's age, and removed the stop date of epoetin zeta.

No follow-up attempts are needed. No further information is expected.

Case Comment: In agreement with the Investigator's opinion, the causality between the events and the study drug was not related.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	30.9 %	
2		Haemoglobin	10.2 g/dl	
3		Red blood cell count	31800	
4		White blood cell count	6500	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	73.7 IU, Freq: 1 Week; Interval: 1, Dose:6000; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	07-AUG-2012 / Unknown; Unknown

Mfr. Control Number: 3084735

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Transient ischaemic attack (Transient ischaemic attack);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
2006 to Ongoing	Relevant Med History type II	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	FINLAND	24	FEB	1947	68 Years	Male	104.00 kg	11	DEC	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: Fatal myocardial infarction. Epoetin zeta. Hospira sponsored study report received from an investigator (ref: Fin-001-0002), which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort
Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included diabetic nephropathy which led to the diagnosis of renal failure in 2000, ischemic heart disease in

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 16-DEC-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 19 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 26-AUG-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CALCICHEW (CALCIUM CARBONATE) ; 15-APR-2013 / Unknown
#2) ETALPHA (ALFACALCIDOL) ; 24-DEC-2012 / Unknown
#3) INNOHEP (TINZAPARIN SODIUM) ; 11-DEC-2015 / Unknown
#4) LASIX /00032601/ (FUROSEMIDE) ; 04-OCT-2015 / Unknown
#5) NOVORAPID (INSULIN ASPART) ; Unknown
#6) PROTAPHANE (INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3137952

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-FEB-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Dec 2015, and peripheral arterial disease. The patient was not on dialysis. The patient had not been treated with an Erythropoesis Stimulating Agent (ESA) before treatment with Retacrit. Concomitant medications included furosemide, Lasix, aspirin, ondansetron 2 mg/ml, Zoloft, Calcichew, alfacalcidol (Etalpha), Protaphane, Novorapid, lisinopril, amlodipine, carvedilol, atorvastatin, Innohep, and bisoprolol. On 26-Aug-2011, the patient started to receive treatment with epoetin zeta (Retacrit, 19 IU/kg/week, 1 dosage/week, frequency also reported as every 10 days, subcutaneous; lot number not known) for renal anaemia. On 15-Apr-2013, the patient was enrolled in the study. On 26 Jun 2015 at 09:49 a.m., P-CRP was at 4 mg/l (normal: less than 3 mg/l) and on 01 Dec 2015 at 08:27 a.m., it was at 3 mg/l. The last dose received by the patient prior to the event was on 04 Dec 2015. On 11 Dec 2015, the patient was admitted to the hospital due to myocardial infarction. On the same day at 06:32 p.m., P-CRP was at 11 mg/l and P-TnT was at 148 ng/l (normal: less than 15 ng/l). On the same day at 02:43 pm, ECG 12 was performed (results not reported). It was stated that on 12-Dec-2015 at 06:14 am ECG12 was again performed (results not reported). P-CRP values were further reported as follows: 10 mg/l in the morning of 12 Dec 2015, 7 mg/l on 14 Dec 2015 at 07:20 a.m., and 18 mg/l in the morning of 15 Dec 2015. On 15 Dec 2015, it was reported that the patient had dyspnea and a feeling of heaviness. Nitroglycerine (dose and route of administration not reported) was at least of temporary help but there were new inferior and anterolateral ST depressions. ECHO examination was then requested which showed, in summary, a decreased systolic dysfunction; apicoseptal as well as clear inferior hypokinesia with no clear valve defects. On the same day at 11:29 am and 02:20 am, ECG was again performed (results not reported). ECG results done on the same day again at 07:25 p.m. were abnormal, which showed an accelerated junctional rhythm, an incomplete LBBB with a significant ST change (a possible inferolateral NSTEMI). It was also reported that compared to the ECG of 12 Dec 2015 at 06:14 a.m., ST depression was enhanced in lead Lateral leads and T inversion was now clearer in lead Lateral leads. In the morning of 16 Dec 2015, PCRP was at 21 mg/l and P-TnT was at 808 ng/l. On 16 Dec 2015 at 06:56 a.m., ECG results were still abnormal which showed junctional rhythm, an incomplete LBBB which was visible compared to the ECG done on the same day at 02:20 a.m., and a significant ST change (possible lateral NSTEMI). It was also reported that compared to the ECG of 16 Dec 2015 at 02:20 a.m., ST depression was now in lead Anterior leads. It was reported that the patient was conservatively treated - no coronary angiography and was resuscitated but it was unsuccessful. Action taken with the suspect drug in response to the event was not reported. The patient died on 16-Dec-2015. Cause of death was myocardial infarction. It was not reported if an autopsy was performed. The investigator considered the event as not related to Retacrit. Risk factors included obesity, hyperlipidaemia, hypertension, diabetes type 2 with diabetic vascular complications, vascular anomalies, aneurysm, immobilisation, recent pregnancy, and positive family history (unspecified). The patient had no coagulation disorders. It was reported that the patient had fluid retention for weeks. The patient was also an ex-smoker.
26 Jan 2016: Additional information was received from the investigator. Patient's complete date of birth was provided; weight and height were updated to 104 kg and 169 cm (previously 108 kg and 175 cm), respectively. . Life-threatening and hospitalization were added as seriousness criteria. Ischemic heart disease, peripheral arterial disease, and fluid retention were added as concurrent conditions. Concomitant medications were provided. Frequency of administration of Retacrit was also reported as every 10 days. Date when the patient received the last dose of Retacrit prior to the event, onset date of the event, and the treatment given were provided. The reporter's opinion of causality was also provided. Obesity, vascular anomalies, aneurysm, immobilisation, recent pregnancy, and positive family history (unspecified) were added as risk factors. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: lot number and previous exposure of patient to other biosimilars. This information has been incorporated in the corresponding data fields and in the narrative. 09 Feb 2016: Translation of the laboratory and diagnostic findings in Finnish text was received. Course of event was updated. Relevant laboratory data included P-CRP and P-TnT values; and the results of ECG done on 15 Dec 2015 and 16 Dec 2015. This information has been incorporated in the corresponding data fields and in the narrative.

Case Comment: Overall case causality: Related Event is possibly related based on temporal relationship and medical plausibility, as Retacrit can theoretically increase the risk of thromboembolic events based on drug mechanism of action, but consider also contributory effects of patient's multiple cardiovascular comorbidities and risk factors. Follow-up: No change in previous causality assessment. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	26-JUN-2015	C-reactive protein	4 mg/l	
2	01-DEC-2015	C-reactive protein	3 mg/l	
3	11-DEC-2015	C-reactive protein	11 mg/l	
4	12-DEC-2015	C-reactive protein	10 mg/l	
5	14-DEC-2015	C-reactive protein	7 mg/l	

Mfr. Control Number: 3137952

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
6	15-DEC-2015	C-reactive protein	18 mg/l	
7	16-DEC-2015	C-reactive protein	21 mg/l	
8	15-DEC-2015	Echocardiogram	No clear valve defects Unknown	
9	15-DEC-2015	Echocardiogram	Decreased systolic dysfunction Unknown	
10	15-DEC-2015	Echocardiogram	Apicoseptal and clear inferior hypokinesia Unknown	
11	11-DEC-2015	Electrocardiogram	Not reported Unknown	
12	12-DEC-2015	Electrocardiogram	Not reported Unknown	
13	15-DEC-2015	Electrocardiogram	ST change, possible inferolateral NSTEMI Unknown	
14	15-DEC-2015	Electrocardiogram	T inversion clearer in lead lateral leads Unknown	
15	15-DEC-2015	Electrocardiogram	ST depression enhanced in lead Lateral leads Unkno	
16	15-DEC-2015	Electrocardiogram	Incomplete LBBB Unknown	
17	15-DEC-2015	Electrocardiogram	Accelerated junctional rhythm Unknown	
18	15-DEC-2015	Electrocardiogram	Not reported Unknown	
19	16-DEC-2015	Electrocardiogram	ST depression in lead Anterior leads Unknown	
20	16-DEC-2015	Electrocardiogram	Junctional rhythm Unknown	
21	16-DEC-2015	Electrocardiogram	Incomplete LBBB Unknown	
22	16-DEC-2015	Electrocardiogram	Not reported Unknown	
23	16-DEC-2015	Electrocardiogram	ST change, possible lateral NSTEMI Unknown	
24	11-DEC-2015	Troponin T	148 NG/L	
25	16-DEC-2015	Troponin T	808 NG/L	

13. Relevant Tests

ECG(15-DEC-2015): ST depression enhanced in lead Lateral leads Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION

Mfr. Control Number: 3137952

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	19 IU/kg, Freq: 1 Week ; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	26-AUG-2011 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ZOLOFT (SERTRALINE HYDROCHLORIDE) ; 01-NOV-2013 / 16-DEC-2015

#8) AMLODIPINE (AMLODIPINE) ; 24-JUL-2013 / Unknown

#9) ASPIRIN /00002701/ (ACETYLSALICYLIC ACID) ; 04-OCT-2010 / Unknown

#10) ATORVASTATIN (ATORVASTATIN) ; 04-OCT-2010 / Unknown

#11) BISOPROLOL (BISOPROLOL) ; 15-DEC-2015 / Unknown

#12) CARVEDILOL (CARVEDILOL) ; 24-JUL-2013 / Unknown

#13) FUROSEMIDE (FUROSEMIDE) ; 11-DEC-2015 / 16-DEC-2015

#14) LISINOPRIL (LISINOPRIL) ; 06-JUL-2015 / 11-DEC-2015

#15) ONDANSETRON (ONDANSETRON) ; 15-DEC-2015 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to the diagnosis of renal failure in 2000, ischemic heart disease in Dec 2015, and peripheral arterial disease. The patient was not on dialysis. The patient had not been treated with an Erythropoesis Stimulating Agent (ESA) before treatment with Retacrit. Risk factors included obesity, hyperlipidaemia, hypertension, diabetes type 2 with diabetic vascular complications, vascular anomalies, aneurysm, immobilisation, recent pregnancy, and positive family history (unspecified). The patient had no coagulation disorders. It was reported that the patient had fluid retention for weeks. The patient was an ex-smoker. Race/Ethnicity: Caucasian The patient died on 16-Dec-2015. Cause of death was myocardial infarction. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Fluid retention (Fluid retention);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Aneurysm (Aneurysm);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Immobile (Immobile);
Unknown	Relevant Med History	Obesity (Obesity);
Unknown	Relevant Med History	Pregnancy (Pregnancy);
Unknown	Relevant Med History	Vascular anomaly (Vascular malformation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	20	APR	1934	81 Years	Male	44.50 kg	30	DEC	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Intracerebral hemorrhage [Cerebral haemorrhage]

Case Description: Intracerebral hemorrhage. Epoetin zeta. Hospira-sponsored study report received from an investigator (reference: Gr-052-0010), which refers to a patient (weight: 44.5 kg also reported as 43 kg). The patient was enrolled in a Hospira-
Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. The patient had no known hypersensitivities and had no history of drug

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 01-JAN-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4X093Z4; Exp.Dt. 01-MAY-2016}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000/3 per week

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 22-MAY-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3168514

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-FEB-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 3168514

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

dependency. Medical history included diabetic nephropathy which led to renal failure diagnosed on 12-May-2011. On the same day, the patient had his first hemodialysis, with an average frequency of 3 times per week. Also on 12-May-2011, the patient was treated with epoetin alpha (Abseamed, 200 IU/kg/week; route of administration not reported) before treatment with Retacrit. The patient had no concomitant medications. On 22-May-2013, the patient started treatment with epoetin zeta (Retacrit, lot number: 4X093Z4, 4000/per week, intravenous also reported as subcutaneous) for renal anaemia. On 13-Mar-2014, the patient was enrolled in the study. On 18-Feb-2014, during week of entry into study, the patient received Retacrit at a dose of 135 IU/kg/week, 2 dosages/week, subcutaneous). On 30-Dec-2015, the patient developed intracerebral hemorrhage. On an unknown date, CT scan was performed (results not reported). Treatment for the event was not reported. Action taken with the suspect drug was not reported; however, therapy end date was on 30-Dec-2015. On 01-Jan-2016, the patient died. Cause of death was intracerebral hemorrhage. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event and the suspect drug was not related. Risk factors included coronary heart disease, atrial fibrillation, hypertension and type 2 diabetes. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars

Case Comment: Overall case causality: Not related Patient has multiple preexistent risk factors and cardiovascular comorbidities.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Computerised tomogram	Not reported, Unknown	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4X093Z4; Exp.Dt. 01-MAY-2016}; Regimen #2	135 IU/kg/week, 2 dosage/week; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	18-FEB-2014 / 30-DEC-2015; 681 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption and tobacco usage were not reported. The patient had no known hypersensitivities and had no history of drug dependency. Medical history included diabetic nephropathy which led to renal failure diagnosed on 12-May-2011. On the same day, the patient had his first hemodialysis, with an average frequency of 3 times per week. Also on 12-May-2011, the patient was treated with epoetin alpha (Abseamed, 200 IU/kg/week; route of administration not reported) before treatment with Retacrit. Risk factors included coronary heart disease, atrial fibrillation, hypertension and type 2 diabetes. On 01-Jan-2016, the patient died. Cause of death was intracerebral hemorrhage. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure); Diagnosed on 12-May-2011
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis); On 12-May-2011, 3 dialysis per week
12-MAY-2011 to Unknown	Past Drug Event	ABSEAMED (ABSEAMED); Drug Indication: Drug use for

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	BULGARIA	03	SEP	1952	63 Years	Female	56.00 kg	01	OCT	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Left hemispheric stroke [Cerebrovascular accident]

Case Description: Fatal left hemispheric stroke. Epoetin zeta. Hospira-sponsored study report received from an Investigator (ref: Bg-015-0017) which refers to a patient. The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of
Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had chronic pielonephritis leading to renal failure (first diagnosed on 16-Jan-2015). The patient was not on dialysis. The patient had not

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 01-OCT-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 109 IU/kg/ (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 27-FEB-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) TOT'HEMA /01122001/ (COBALT GLUCONATE, COPPER GLUCONATE, CYANOCOBALAMIN, FERROUS GLUCONATE, LIVER EXTRACT, MANGANESE GLUCONATE, SODIUM BENZOATE) ; 04-SEP-2015 / 01-OCT-2015

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic pyelonephritis (Pyelonephritis chronic)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3181623

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-FEB-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 3181623

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

received any other erythropoietin stimulating agents (ESA) before treatment with Retacrit. Concomitant medication included Tot'hema. On 27-Feb-2015, the patient started treatment with epoetin zeta (Retacrit, 109 IU/kg/week, two dosages per week, subcutaneous, batch number unknown) for anemia. On an unknown date in 2015, the patient's WBC showed 11.3 x10^9/L (normal values: 3.5-10.5), Hb was 83 g/L (normal values: 120-180), RBC was 3.35 x 10^12/L (normal values: 4.20-6.20) and PLT was 282 x10^9/L (normal values: 140-440). On an unknown date, the patient's urea was 24.2 mmol/L (normal value: less than or equal to 8.3) and creatinine was 468 micromol/L (normal values: 44-134). On 01-Oct-2015, the patient experienced left hemispheric stroke. It was reported that there was no treatment for the event. Action taken with the suspect drug in response to the adverse event was not reported. Date of last dose of Retacrit administered to the patient was on 29-Sep-2015. The patient died on the same day of 01-Oct-2015. Cause of death was left hemispheric stroke. It was unknown if an autopsy was performed. The reporter's opinion of causality between the event and the suspect drug was unlikely. It was also reported that the event of left hemispheric stroke was not an adverse reaction. Risk factors included hypertension and diabetes type 2 without vascular complications, both since 2002.
The following information has been requested from the reporter for identification and traceability of the biosimilar product: previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Related Event is possibly related based on medical plausibility as the suspect drug can theoretically increase the risk of thromboembolic events. Consider also possible contributory effects from cardiovascular risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood creatinine	468 MCMOL/L	134 44
2		Blood urea	24.2 mmol/l	
3	01-JAN-2015	Haemoglobin	83 g/l	180 120
4	01-JAN-2015	Platelet count	282 x10 9/l	440 140
5	01-JAN-2015	Red blood cell count	3.35 x10 12/l	6.20 4.20
6	01-JAN-2015	White blood cell count	11.3 x10 9/l	10.5 3.5

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	109 IU/kg/week, Freq: 2 Week; Interval:1; Subcutaneous	Anemia (Anaemia)	27-FEB-2015 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. The patient had chronic pielonephritis leading to renal failure (first diagnosed on 16-Jan-2015). The patient was not on dialysis. The patient had not received any other erythropoietin stimulating agents (ESA) before treatment with Retacrit. Race/Ethnicity: Caucasian The patient died on the same day of 01-Oct-2015. Cause of death was left hemispheric stroke. It was unknown if an autopsy was performed. Risk factors included hypertension and diabetes type 2 without vascular complications, both since 2002.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure); First diagnosed on 16-Jan-2015
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

Mfr. Control Number: 3181623

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Risk Factor-2002	
Unknown	Relevant Med History	Hypertension (Hypertension);
	Risk Factor-2002	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	17	MAY	1929	86 Years	Male	65.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Coronary infarction [Myocardial infarction]

Case Description: Fatal coronary infarction. Epoetin zeta. Hospira-sponsored study report received from an Investigator (ref: Gr-065-0005), which refers to a patient. The patient was enrolled in the Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient's medical history included hypertensive nephropathy which leads to renal failure on 30-Dec-2013. The patient had an abdominal aortic aneurysm operation in 1994.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 29-OCT-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 85 IU/kg,weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-AUG-2015 / 29-OCT-2015	#1) 70 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CLOPIDOGREL (CLOPIDOGREL) ; Unknown
#2) EZETIMIBE W/SIMVASTATIN (EZETIMIBE, SIMVASTATIN) ; Unknown
#3) OMEPRAZOLE (OMEPRAZOLE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)
30-DEC-2013 to Ongoing	Relevant Med History	Renal failure (Renal failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3272375

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
12-MAY-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

It was reported that the patient suffered from coronary artery disease since 1995, and had a coronary artery bypass grafting on the same year. Heart failure from an unknown date and unknown if ongoing, ongoing hyperlipidaemia under medication, ongoing hypertension, myocardial infarction from an unknown date and unknown if ongoing, peripheral arterial disease from an unknown date and unknown if ongoing. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications included clopidogrel, simvastatin, and omeprazole. On 21-Aug-2015, the patient started treatment with epoetin zeta (Retacrit; 85 IU/kg/week,1 dosages/week, subcutaneous; lot number unknown) for renal anaemia. The patient was enrolled in the study and signed informed consent on 21-Aug-2015. On an unknown date, the patient experienced coronary infarction. On 29-Oct-2015, the patient died. Cause of death was reported as coronary infarction. It was reported that autopsy was not performed. The Investigator's opinion of causality between the events and the suspect drug was not related. Risk factors included coronary heart disease, myocardial infarction, peripheral arterial disease, hyperlipidaemia, hypertension, heart failure and current smoker. 05 May 2016: Additional information was received from the same reporter. It was reported that the patient had coronary artery bypass grafting in 1995 and abdominal aortic aneurysm operation in 1994. Concomitant medications were added. It was reported that autopsy was not performed. Reporter's causality was updated to not related (previously reported as not provided). This information has been incorporated in the narrative and in the corresponding data fields. The reporter was not able to provide the following information for identification and traceability of the biosimilar product Retacrit: lot number and date of expiry.

Follow-up (12May2016). No narrative was provided by the investigator. New information received from the investigator includes:

POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study source for Protocol ID EPOE-09-11, Center ID/Subject ID 065|0005.

The 86-years-old Caucasian male patient started to receive epoetin zeta (RETACRIT) subcutaneously on 21Aug2015 at 85 IU/Kg, weekly for renal anemia. The patient was smoking for more than 65 years. Relevant medical history was as in the initial report. Concomitant medications included clopidogrel (CLOPIDOGREL) at 75 mg, daily, simvastatin and ezetimibe (EZETIMIBE W/SIMVASTATIN) at 10-10, daily and omeprazole (OMEPRAZOLE) at 20 mg, daily. The patient underwent laboratory examination on 21Aug2015 and 07Oct2015 that showed haemoglobin 10 g/dl and 10.9 g/dl respectively. Also on an unspecified date the patient's haematocrit was 32.1 (no units provided).

The investigator considered that the adverse event was not related to the suspect drug epoetin zeta.

No further information expected. No more info needed.

Case Comment: Overall case causality: Possible (reporter causality not provided) Hospira causality: Not related Although the suspect drug can theoretically increase the risk of thromboembolic events, the patient's multiple risk factors and preexistent comorbidities far outweigh the potential risk from the drug as patient was on the medication for just two months. Follow-up: No change in assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	32.1	
2	21-AUG-2015	Haemoglobin	10 g/dl	
3	07-OCT-2015	Haemoglobin	10.9 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1994 to Unknown	Relevant Med History	Aortic aneurysm repair (Aortic aneurysm repair); had an operation in 1994 for abdominal aortic aneurism
1995 to Unknown	Relevant Med History	Coronary artery bypass graft (Coronary artery bypass);
1995 to Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Heart failure (Cardiac failure);

Mfr. Control Number: 3272375

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History under medication	Hyperlipidaemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History for more than 65 years	Smoker (Tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SWEDEN	01	SEP	1933	82 Years	Male	73.00 kg	23	APR	2016	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Sepsis due to dialysis catheter [Sepsis]
Acute infarction [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This case has been migrated from another database into the current safety database for processing follow-up information.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 26-APR-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 10000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 22-MAY-2014 / 19-APR-2016	#1) 699 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INOLAXOL (STERCULIA URENS) ; 19-JAN-2011 / Ongoing
#2) NOVOMIX (INSULIN ASPART, INSULIN ASPART PROTAMINE (C
#3) ETALPHA (ALFACALCIDOL) Capsule ; 24-NOV-2013 / Ongoing
#4) ORALOVITE (ASCORBIC ACID, NICOTINAMIDE, PYRIDOXINE H
#5) KALCIDON (CALCIUM CARBONATE) Chewable tablet ; 13-MAY-2013 / Ongoing
#6) INNOHEP (TINZAPARIN SODIUM) Solution for injection ; 06-AUG-2014 / 22-APR-2016 **(Continued on Additional Information Page)**

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)
10-DEC-2012 to Ongoing	Relevant Med History	Renal failure (Renal failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3291130

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-OCT-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

This is a non-interventional study report, protocol EPOE-09-11, regarding subject SW005|0039. Fatal sepsis due to dialysis catheter. Epoetin zeta. Hospira sponsored study report received from an Investigator, which refers to a subject (ref: Sw-005-0039). The subject was enrolled in a Hospira-Sponsored Post Authorization Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The subject was diagnosed with diabetic nephropathy that led to renal failure on 10 Dec 2012. The subject was on dialysis since 19 Nov 2013 for 3 dialysis per week. The subject received darbepoetin alfa (Aranesp, 460 ng/kg/week) for an unknown indication on 22 Oct 2013. Concomitant medication was not reported. On 22 May 2014, the subject began treatment with epoetin zeta (Retacrit; 129 IU/kg/week, 1 dosage per week, subcutaneous) for renal anaemia. On an unknown date, the subject experienced sepsis due to dialysis catheter. Investigations including examinations, laboratory and diagnostic data, treatment and action taken with the suspect drug were not reported. On 24 Apr 2016, the subject died. Cause of death was sepsis due to dialysis catheter. It was not reported if an autopsy was performed. The reporter's opinion of causality between the event and the suspect drug was not related. Risk factors included coronary heart disease, myocardial infarction, hyperlipidaemia, hypertension, and diabetes type I with diabetic vascular complications. The subject was a smoker. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: batch number, date of expiry, previous exposure of subject to other biosimilars.

Follow-up (10Oct2016): New information includes: AESI/Death reason: Acute heart infarction (as documented on the death certificate). Previous reason documented in the cCRF: sepsis due to dialysis catheter not related to Retacrit. Death date 24Apr2016.

Follow-up (17Oct2016): New information included: The subject was hospitalized due to Staphylococcus aureus sepsis from 23Apr2016 to 26Apr2016. Decision was taken to restrict the measures of care and the subject was moved from the intensive care unit to the medical observation department (MOA). No dialysis, respirator intensive care or CPR (cardiopulmonary resuscitation). The subject died as a result of this, acute myocardial infarction (AMI) at 1:30 p.m. on 26Apr2016. AMI was not 100 percent certain cause of death, but was found at autopsy. The subject's sepsis strong contributing to the cause. Additional information: Death date was changed to 26Apr2016 (from 24Apr2016). Cause of death was updated as determined by autopsy. Autopsy results added: Terminal cause of death was acute myocardial infarction that was caused by diabetes with atherosclerosis. Other diseases that contributed to the death were chronic kidney failure with hemodialysis and diabetes with kidney disease. Weight and height was reported. Updated information in medical history (diabetes onset 1970, below knee amputation 2007 and MI in 1981 and in 2005, bypass operation 2006, cardiac failure from 2006; hypertension onset 1990, hyperlipidemia onset 1990 approximately; claudicatory added, onset approximately 1990. Concomitant medications were now reported. Updated information for the study drug: 10000 IU once a week, stop date 19Apr2016. The subject received treatment on 26Apr2016 with cloxacillin 2 gram/100 ml concentration 0.02 gram/ml: 200 ml/h for 30 minutes 3 infusions per day; and ipratropium/salbutamol (SAPIMOL) 0.5 mg/2.5 mg per 2.5 ml; 2.5 ml (one single-dose container) three times per day. As concomitant medication the subject had also from 20Nov2013 DuraLock 2.2ml in connection with the dialysis. Laboratory results added for 26Apr2016.

Follow-up (27Oct2016): New information included: All concomitant medications were ongoing apart from Innohep injection fluid 10000 IU/ml, that was stopped on 22Apr2016. Onset date for sepsis was 23Apr2016. Updated information in medical history (angina, gout, asthma, COPD, high eye pressure). Acute myocardial infarction resulted in death, was added as new event with onset date of 26Apr2016. This event was not related to study medication or to concomitant medication. Action taken with study drug in response to the event was not applicable.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported events were related to the study drug Retacrit (EPOETIN ZETA). The events were most likely due to intercurrent or underlying conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	26-APR-2016	Activated partial thromboplastin time	43 seconds	32 24
2	26-APR-2016	Anti-thrombin antibody	0.50	1.25 0.85
3	26-APR-2016	Aspartate aminotransferase	1.4	<0.76
4	26-APR-2016	Base excess	-4.4 mmol/l	3.0 -3.0
5	26-APR-2016	Blood creatinine	304 umol/l	105 60
6	26-APR-2016	Blood fibrinogen	1.4 g/l	4.0 2.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	26-APR-2016	Blood glucose	3.0 mmol/l	10.9 4.2
8	26-APR-2016	Blood pH	7.26	7.45 7.36
9	26-APR-2016	Blood phosphorus	1.5 mmol/l	1.4 0.75
10	26-APR-2016	Blood urea	14.7 mmol/l	8.2 3.5
11	26-APR-2016	C-reactive protein	24 mg/l	<10
12	26-APR-2016	Carbon dioxide	6.6	6.0 4.7
13	26-APR-2016	Fibrin D dimer	1.1 mg/l	<0.25
14	26-APR-2016	Glomerular filtration rate	17	>45
15	26-APR-2016	Haematocrit	0.35	0.50 0.40
16	26-APR-2016	Haemoglobin	113 g/l	170 134
17	26-APR-2016	Haemoglobin	118 g/l	170 134
18	26-APR-2016	Hydrogen breath test	7.26	7.45 7.36
19	26-APR-2016	International normalised ratio	1.4	1.2 0.8
20	26-APR-2016	Mean cell haemoglobin	35 pg	33 27
21	26-APR-2016	Mean cell volume	107	98 82
22	26-APR-2016	Oxygen saturation	92.7 %	>95
23	26-APR-2016	PO2	9.8	13.5 10.0
24	26-APR-2016	Platelet count	52 x10 9/l	350 140
25	26-APR-2016	Procalcitonin	7.4	<0.5
26	26-APR-2016	Red blood cell count	3.3 x10 12/l	5.7 4.3
27	26-APR-2016	White blood cell count	13.5 x10 9/l	8.8 3.5

13. Relevant Tests

Haematocrit (B-EVF): (26Apr2016): 0.35 (0.40-0.50) No units provided.
P-antithrombin (enz, Tromb) (26Apr2016): 0.50 kIU/L (ref.0.85-1.25)
Mean cell volume (B-MVC) (26Apr2016): 107 fL (ref. 82-98)
Aspartate aminotransferase (P-AST) (26Apr2016): 1.4 ukat/L (ref. <0.76)
P-Procalcitonin (26Apr2016): 7.4 ug/L (ref. <0.5)
Pt-Crea,eGFR, MDRD (Relative GFR): 17 ml/min/1.73m2. (ref >45)
aB-carbon dioxide(pCO2): 6.6 kPa (4.7-6.0)
aB-Oxygen (pO2): 9.8 kPa (10.0-13.5).

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) NOVOMIX (INSULIN ASPART, INSULIN ASPART PROTAMINE (CRYSTALLINE)) ; 06-AUG-2014 / Ongoing

#4) ORALOVITE (ASCORBIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) Tablet ; 29-NOV-2013 / Ongoing

#7) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; 21-JUL-2009 / Ongoing

#8) COSMOFER (IRON DEXTRAN) ; 19-NOV-2013 / Ongoing

#9) IMDUR (ISOSORBIDE MONONITRATE) Prolonged-release tablet ; 14-JUN-2013 / Ongoing

#10) FURIX (FUROSEMIDE) ; 17-FEB-2016 / Ongoing

#11) METOPROLOL SANDOZ (METOPROLOL TARTRATE) Prolonged-release tablet ; 21-JUL-2009 / Ongoing

#12) AMLODIPIN ACCORD (AMLODIPINE BESILATE) ; 03-SEP-2014 / Ongoing

#13) CAPTOPRIL ACTAVIS (CAPTOPRIL) ; 23-FEB-2015 / Ongoing

#14) SIMVASTATIN BLUEFISH (SIMVASTATIN) Film-coated tablet ; 11-MAR-2015 / Ongoing

#15) CANODERM (UREA) ; 01-JUN-2010 / Ongoing

#16) LOCOID (HYDROCORTISONE BUTYRATE) ; 27-JAN-2016 / Ongoing

#17) ALLOPURINOL (ALLOPURINOL) ; 06-JAN-2015 / Ongoing

#18) FORMATRIS (FORMOTEROL FUMARATE) ; 11-NOV-2014 / Ongoing

#19) SPIRIVA (TIOTROPIUM BROMIDE) Inhalation powder, hard capsule ; 13-MAY-2014 / Ongoing

#20) AZOPT (BRINZOLAMIDE) Eye drops, suspension ; 13-MAR-2013 / Ongoing

#21) DUOTRAV (TIMOLOL MALEATE, TRAVOPROST) Eye drops, solution ; 22-AUG-2011 / Ongoing

#22) RESONIUM (SODIUM POLYSTYRENE SULFONATE) Powder for oral suspension ; 25-AUG-2015 / Ongoing

#23) RENVELA (SEVELAMER CARBONATE) Film-coated tablet ; 18-JUL-2013 / Ongoing

#24) XERODENT (SODIUM FLUORIDE, XYLITOL) Lozenge ; 02-SEP-2014 / Ongoing

#25) NOVORAPID (INSULIN ASPART) ; 06-AUG-2014 / Ongoing

#26) ACTILYSE (ALTEPLASE) ; 23-FEB-2014 / Ongoing

#27) NITROLINGUAL (GLYCERYL TRINITRATE) Sublingual spray ; 16-NOV-2011 / Ongoing

#28) VENTILASTIN (SALBUTAMOL SULFATE) ; 20-DEC-2012 / Ongoing

#29) ACETYLCYSTEIN (ACETYLCYSTEINE) ; 18-FEB-2016 / Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
19-NOV-2013 to Unknown	Relevant Med History	Dialysis (Dialysis);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
1970 to Ongoing	Relevant Med History	Type 1 diabetes mellitus (Type 1 diabetes mellitus);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
1990 to Ongoing	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
1990 to Ongoing	Relevant Med History	Hypertension (Hypertension);
1981 to Unknown	Relevant Med History and 2005	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Smoker (Tobacco user);
22-OCT-2013 to Unknown	Past Drug Event 460 ng/kg/ week	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
2006 to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
2007 to Unknown	Relevant Med History	Below knee amputation (Leg amputation);
2006 to Unknown	Relevant Med History	Bypass surgery (Vascular graft);
1990 to Ongoing	Relevant Med History	Claudication (Intermittent claudication);
2013 to Ongoing	Relevant Med History	Angina pectoris (Angina pectoris);
2006 to Ongoing	Relevant Med History	Gout (Gout);
2011 to Ongoing	Relevant Med History <2011	Asthma (Asthma);
2011 to Ongoing	Relevant Med History <2011	COPD (Chronic obstructive pulmonary disease);
2009 to Ongoing	Relevant Med History <2009	Intraocular pressure high (Intraocular pressure increased);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	CROATIA	18	NOV	1936	79 Years	Female	55.00 kg	09	MAY	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri [Fall]
Head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri [Subdural haematoma]
Head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri [Brain oedema]
Head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri [Coma]

Case Description: This case has been migrated from another database into

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 11-MAY-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2J305K2}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 29-OCT-2014 / 07-MAY-2016

19. THERAPY DURATION
#1) 557 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CORDIPIN XL (NIFEDIPINE) Tablet ; Unknown
#2) TRANDOLAPRIL (TRANDOLAPRIL) Tablet ; Unknown
#3) EBRANTIL /00631801/ (URAPIDIL) Tablet ; Unknown
#4) FURSEMID /00032601/ (FUROSEMIDE) Tablet ; Unknown
#5) ROCALTROL (CALCITRIOL) ; Unknown
#6) KCL (POTASSIUM CHLORIDE) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1997 to Unknown	Relevant Med History	Cholecystectomy (Cholecystectomy)
Unknown to Ongoing	Relevant Med History for years	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016267631

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-JUN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

the current safety database for processing follow-up information. As a consequence of this migration, the follow-up CIOMS I or MedWatch report may indicate in the appropriate field that it is an initial report.

POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Non-Interventional Study report, protocol EPOE-09-11, regarding subject CR-005-0014. This subject of unspecified gender, age and ethnicity started to receive Epoetin Zeta injections, dosage and start date unspecified, for renal anemia. The subject's medical history and concomitant medications were not reported. On 11May2016, the subject died due to head trauma due to downfall, subdural hematoma, oedema cerebri, after neurosurgical treatment. The action taken with the study drug was unknown. No causality assessment was provided.

Follow-up (24May2016): New information received from the investigator includes: patient details (initials, DOB, age: 79 years, height, weight, gender: female), event details (SAE term reported as death due to downfall, subdural haematoma, oedema cerebri, died after neurosurgical treatment; onset date reported as 09May2016 13:04, stop date 11May2016, last dose prior to onset: 07May2016 10:00, autopsy wasn't done, cause of death reported as haematoma subdurale, coma cerebri); suspect drug details (Retacrit subcutaneously at 6000 IU, 2x/day from 29Oct2014 to 07May2016 for anemia, nifedipine (CORDIPIN XL) tablets orally at 40 mg, 2x/day for hypertension, trandolapril tablet orally at 2 mg, 1x/day for hypertension, urapidil (EBRANTIL) tablet orally at 30 mg, 2x/day for hypertension, fursemidr tablets orally at 40 mg, 1x/day as needed for diuretic therapy, calcitriol (ROCALTROL) orally at 0.5 ug, 1x/day for renal bone disease; action taken for all suspect drugs reported as none and causality as not related, dechallenge/rechalenge reported as not applicable). Concomitant drugs, relevant history and laboratory test extracted from medical records attached to report: relevant history included cholecystectomy on 1997, hypertension for years, transition cell carcinoma of right kidney, pyelon resection on 2006, nephroureterectomy on 2012 on the right side due to remission, bladder carcinoma, dialysis from 2014 due to renal insufficiency. Concomitant drugs included KCl 1 tablet per day and 2 tablets per day during dialysis, calcium carbonate 1 g, carbohydrates NOS/ fats NOS/ minerals NOS/ protein/ vitamins NOS (NEPRO HP) at 1 DF during the day. Lab test section was updated with relevant tests provided.

The following narrative was provided: Transported to hospital by emergency unit, found at home unconscious, GCS 4 (1,1,2), RR 130/95, C/P 90/min. MR cerebri finding: subdural haematoma right, neurological finding: diagnosis: haematoma subdurale, coma cerebri. Transported to neurosurgical unit. Patient died after neurosurgical treatment.

Follow-up (03Jun2016): New information received from the investigator includes completed DCA questionnaire with the following new information received: patient details (weight updated to 55,5 kg, ethnicity: Caucasian, type of dialysis updated to haemodialysis), suspect drug details (Retacrit lot number: 2J305K2, frequency of administration updated to 2x week, mean dose 1 on 17Feb2015 was 6000 IU with haemoglobin: 99 g/l; mean dose 2 on 16Mar2016 was 6000 IU with haemoglobin: 102 g/l on 13Apr2016; there haven't been any dose changes within 3 months prior to event; patient was previously taking other ESA- Neorecormon from 24Jan2014 to 25Oct2014 at 4000 IU and didn't experience any thromboembolic events during that treatment). The patient didn't have any of the risk factors for thromboembolic events listed in the questionnaire, while among the listed relevant concurrent and past diseases the patient had only hypertension and right side renal carcinoma from 2006 to 19May2012 when right side nephrectomy was done. Event term was updated to 'head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri', stop date was reported as 11May2016, causality reported as unrelated, the patient was hospitalized due to the event from 09May2016 to 11May2016, treatment of the event included neurosurgery treatment. The following products, previously reported as suspect were reported as concomitant drugs: Cordipin XL, Trandolapril, Ebrantil, Fursemid, Rocaltrol. The following lab test were reported: haemoglobin (101 g/l on 09May2016, 102 g/l on 13Apr2016, 99 g/l on 17Feb2016), haematocrit (35% on 09May2016, 35,4% on 13Apr2016, 32,6% on 17Feb2016), red blood cells (3.52x 10 12/l on 09May2016, 3.41 x 10 12/l on 13Apr2016), CRP (2.8 mg/l on 09May2016, 19.5 mg/l on 13Apr2016, 135.7 mg/l on 17Feb2016), leucocytes (16.3x 10 9/l on 09May2016, 6.3x 10 9/l on 13Apr2016, 13.5x 10 9/l on 17Feb2016), brain MRI on 09May2016: subdural hematoma right, neurological exam on 09May2016: subdural hematoma, coma cerebri.

Follow-up attempts are completed. No new information is expected.

Case Comment: The reported events, head trauma due to downfall, subdural hematoma, oedema cerebri, coma cerebri, likely represent intercurrent and/or underlying medical conditions in this elderly patient with multiple comorbidities. The events are assessed as unrelated to the study drug or concomitant medications.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09-MAY-2016	Activated partial thromboplastin time	23.1	
2	09-MAY-2016	Blood creatine phosphokinase	88 IU/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
3	09-MAY-2016	Blood creatinine	373 umol/l	
4	09-MAY-2016	Blood fibrinogen	2.6 g/l	
5	09-MAY-2016	Blood glucose	7.7 mmol/l	
6	09-MAY-2016	Blood lactate dehydrogenase	220 IU/l	
7	09-MAY-2016	Blood potassium	4.9 mmol/l	
8	09-MAY-2016	Blood pressure measurement	130/95 mmHg	
9	09-MAY-2016	Blood sodium	141 mmol/l	
10	09-MAY-2016	Blood urea	21.6 mmol/l	
11	17-FEB-2016	C-reactive protein	135.7 mg/l	
12	13-APR-2016	C-reactive protein	19.5 mg/l	
13	09-MAY-2016	C-reactive protein	2.8 mg/l	
14	09-MAY-2016	Coma scale	4 (1,1,2)	
15	17-FEB-2016	Haematocrit	32.6 %	
16	13-APR-2016	Haematocrit	35.4 %	
17	09-MAY-2016	Haematocrit	35 %	
18	17-FEB-2016	Haemoglobin	99 g/l	
19	13-APR-2016	Haemoglobin	102 g/l	
20	09-MAY-2016	Haemoglobin	101 g/l	
21	09-MAY-2016	International normalised ratio	0.9	
22	09-MAY-2016	Magnetic resonance imaging brain	subdural hematoma on the right side	
23	09-MAY-2016	Magnetic resonance imaging brain	subdural hematoma right	
24	09-MAY-2016	Mean cell haemoglobin	28.7 pg	
25	09-MAY-2016	Mean cell haemoglobin concentration	289 g/l	
26	09-MAY-2016	Mean cell volume	99.3	
27	09-MAY-2016	Mean platelet volume	9	
28	09-MAY-2016	Neurological examination	hematoma subdural, coma cerebral	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
29	09-MAY-2016	Platelet count	246 x10 9/l	
30	09-MAY-2016	Prothrombin time	1.15	
31	17-FEB-2016	Red blood cell count	x10 12/l	
32	13-APR-2016	Red blood cell count	3.41 x10 12/l	
33	09-MAY-2016	Red blood cell count	3.52 x10 12/l	
34	09-MAY-2016	Red cell distribution width	17.6 %	
35	17-FEB-2016	White blood cell count	13.5 x10 9/l	
36	13-APR-2016	White blood cell count	6.3 x10 9/l	
37	09-MAY-2016	White blood cell count	16.3 x10 9/l	

13. Relevant Tests

C/P (09May2016): 90/min
Neurological exam (09May2016): subdural hematoma, coma cerebri

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) CALCIUM CARBONATE (CALCIUM CARBONATE) ; Unknown

#8) NEPRO /07459601/ (CARBOHYDRATES NOS, FATS NOS, MINERALS NOS, PROTEIN, VITAMINS NOS) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2006 to 19-MAY-2012	Relevant Med History right kidney Carcinoma renis dex	Transitional cell carcinoma (Transitional cell carcinoma);
2006 to Unknown	Relevant Med History	Bladder neck resection (Bladder neck resection);
19-MAY-2012 to Unknown	Relevant Med History -on the right side -nephrectomia renis dex	Nephroureterectomy (Nephroureterectomy);
Unknown	Relevant Med History	Bladder carcinoma (Bladder cancer);
2014 to Unknown	Relevant Med History due to renal insufficiency	Haemodialysis (Haemodialysis);
24-JAN-2014 to 25-OCT-2014	Past Drug Event - 4000 IU	Neorecormon (NEORECORMON); Drug Indication: Product used for unknown indication (Product used for unknown indication), Drug Reaction: No adverse effect (No adverse event)
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	ITALY	26	JUN	1932	83 Years	Male	75.00 kg	19	MAR	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)
This is a report from a Non-Interventional Study source for Protocol EPOE-09-11, Center ID IT116, Subject ID 0018.
An 83-year-old male Caucasian patient started to receive epoetin zeta (RETACRIT), subcutaneous from 12Nov2012 to an unspecified date at 4000

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 19-MAR-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 4000 IU/5 days

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) RENAL ANAEMIA (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 12-NOV-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CALCITRIOL (CALCITRIOL) ; Unknown
#2) ARIXTRA (FONDAPARINUX SODIUM) ; 11-FEB-2016 / Unknown
#3) HUMALOG (INSULIN LISPRO) ; Unknown
#4) CARDIOASPIRINA (ACETYLSALICYLIC ACID) ; 11-FEB-2016 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
FEB-2014 to Unknown	Relevant Med History	Peritoneal dialysis (Peritoneal dialysis)
12-NOV-2012 to 08-MAR-2013	Past Drug Event 2000 IU/week	Neorecormon (NEORECORMON)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016281626

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
29-JUN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

IU/5 days for renal anaemia. There were two independent values of mean doses applied within the period of 3 months prior to the event: Mean dose 1 at 4000 x 2 IU/10 days 18Jan2016, Hb 12.5 g/dl and Mean dose 2 at 4000 IU/5 days 04Mar2016, Hb 9.7 g/dl. There had been dose changes within 3 months prior to the event on 04Mar2016, new dose was 4000 IU/5 days Hb prior to dose change was 9.7 g/dl. The subject had been exposed to other erythropoietin-stimulating agent (ESA) which included epoetin beta (NEORECORMON) from 12Nov2012 to 08Mar2013 at 2000 IU/week; Hb 10.5 g/dl. The subject did not experience any thromboembolic event during treatment with any other ESA. Medical history: patient treated for chronic renal failure in automated peritoneal dialysis since Feb2014. For some months, patient had cognitive impairment with several entrances at ER. He was evaluated by neurologist and acetylsalicylic acid (CARDIOASPIRIN) was added to therapy with low molecular weight heparins. Risk factors included ex-smoker (smoking from an unknown date to 1965), atrial fibrillation (AF), and myocardial infarction in 2006. Relevant concurrent and past disease included ongoing hyperlipidemia, ongoing ischemic heart disease, transient ischaemic attack in 1988 (recovered), ongoing peripheral arterial disease, diabetes mellitus and hypertension from 1988 and ongoing, ongoing atrial fibrillation.

Concomitant medications included calcitriol 0.25 mcg daily, fondaparinux sodium (ARIXTRA, strength 1.5) one vial subcutaneously at 6 pm (daily) from 11Feb2016, acetylsalicylic acid (CARDIOASPIRINA) one dose form (DF) daily after lunch from 11Feb2016 and insulin lispro (HUMALOG). The subject was hospitalized from 27Feb2016 to 04Mar2016 with the diagnosis of rectal bleeding in chronic uremic patient receiving automated peritoneal dialysis, cerebral ischemic vascular disease with previous stroke, type 2 diabetes mellitus, ischemic-hypertensive heart disease with hypokinetic evolution, chronic atrial fibrillation. On 27Feb2016, he developed rectal bleeding and for this reason he presented at Emergency room and then hospitalized. Objective examination included blood pressure (BP) 105/70 mmHg; Heart rate (HR) 110/min; body weight 75 kg. Arrhythmic cardiac activity, tachycardia. Chest: vesicular murmur extensively reduced. Abdomen treatable, peristalsis present. No edema in lower extremity. At discharge (04Mar2016): BP 130/70 mmHg; body weight 74 kg. Lab tests at entrance included: red blood cell sedimentation rate (ESR) 83, glycated hemoglobin 9.6 %, azotemia 133, creatinine 7.4, serum uric acid 7.9, sodium 139, potassium 5.2, calcium 9.9, red blood cell count (RBC) 3380000, Hb 10.8 g/dl, Hematocrit 32.3, mean cell volume 95.6, white blood cell count (WBC) 8020, platelet 267000, prothrombin time 85%, activated partial thromboplastin time 32, aspartate aminotransferase (SGOT) 11, alanine aminotransferase (SGPT) 11, gamma-glutamyl transferase (GGT) 44, alkaline phosphatase 118, lactate dehydrogenase (LDH) 495, protein total 6.4, albumin 3 g, alfa 1 6.5, alfa 2 17.4, beta 14.3 gamma 14.7, C-Reactive Protein (CRP) 45.5, Carcinoembryonic Antigen (CEA) 3.7, calcium (Ca) 19-9 12, fibrinogen 652, antithrombin 100. Lab tests at discharge included sodium 139, potassium 4.5, RBC 3120000, hemoglobin (Hb) 9.7, hematocrit 29.5, mean cell volume 94.6, WBC 7580 (Neu 61.5, Lymph 25.7, Mono 9.9, Eo 2.2, Basophils 0.7 %), platelet 219000. On 28Feb2016, electrocardiogram (ECG) showed AF tachycardic, signs of SVS/ischemia already known. On 27Feb2016 abdomen ultrasound (test performed in Emergency/urgency and restricted due to intestinal meteorism) showed Acalculous gallbladder and bile ducts explorable, not dilated. Kidneys reduced in size and with cysts, no signs of bilateral hydronephrosis. Abdominal aorta atheromatous, normal caliber in explorable tracts. Not effusion in the peritoneal recesses. On 27Feb2016, abdomen X-ray showed not significant hydrogas levels nor signs of pneumoperitoneus. Catheter for peritoneal dialysis in left iliac fossa. Diffuse vascular calcifications. On 02Mar2016 rectoscopy showed polyp of sigma colon. During hospitalization there were no additional episodes of bleeding. Resection of the polyp was scheduled on 04Mar2016 but it was not performed due to failure to view the polyp. The patient experienced myocardial infarction and died on 19Mar2016. The action taken in response to the event myocardial infarction with epoetin zeta was unknown. The patient died on 19Mar2016. It was not reported if an autopsy was performed.

The investigator considered there was not a reasonable possibility that the event was related to suspect product.

Follow-up (07Jun2016): Additional information received from site included patient's details (gender, age, weight, height), causality assessment (unrelated), suspect drug details (trade name, start date, dosage and frequency, route of administration). No drug hypersensitivities. No drug dependence.

Follow-up (08Jun2016): New information received from the site includes updated patient's age, ethnicity provided, suspect product trade name, medical history, concomitant medications, relevant tests.

Follow-up (28Jun2016): New information received from the site includes concomitant medications (Cardioaspirina was started on 11Feb2016 along with Artixtra).

Follow-up (29Jun2016): New information received from the site includes concomitant medications (the dosages of Cardioaspirina and Artixtra).

Case Comment: Based on available information, the company considered that there was not a reasonable possibility that the reported event myocardial infarction with death out come was related to study medication. Underlying diseases of hyperlipidemia, ischemic heart disease, atrial fibrillation, diabetes mellitus and hypertension were regarded as predisposing factors in causing the event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	27-FEB-2016	Abdominal X-ray	Not significant hydrogas levels	
2		Activated partial thromboplastin	32	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		time		
3		Alanine aminotransferase	11	
4		Antithrombin III	100	
5		Aspartate aminotransferase	11	
6		Azotaemia	133	
7	04-MAR-2016	Basophil count	0.7 %	
8		Blood albumin	3 g	
9		Blood alkaline phosphatase	118	
10		Blood calcium	9.9	
11		Blood creatinine	7.4	
12		Blood fibrinogen	652	
13		Blood lactate dehydrogenase	495	
14		Blood potassium	5.2	
15	04-MAR-2016	Blood potassium	4.5	
16		Blood pressure measurement	105/70 mmHg	
17	04-MAR-2016	Blood pressure measurement	130/70 mmHg	
18		Blood sodium	139	
19	04-MAR-2016	Blood sodium	139	
20		Blood uric acid	7.9	
21		C-reactive protein	45.5	
22		Carbohydrate antigen 19-9	12	
23		Carcinoembryonic antigen	3.7	
24	28-FEB-2016	Electrocardiogram	tachycardia	
25	04-MAR-2016	Eosinophil count	2.2	
26		Gamma-glutamyltransferase	44	
27		Glycosylated haemoglobin	9.6 %	
28		Haematocrit	32.3	

Mfr. Control Number: 2016281626

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
29	04-MAR-2016	Haematocrit	29.5	
30		Haemoglobin	10.8 g/dl	
31		Haemoglobin	10.5 g/dl	
32	18-JAN-2016	Haemoglobin	12.5 g/dl	
33	04-MAR-2016	Haemoglobin	9.7 g/dl	
34		Heart rate	110	
35	04-MAR-2016	Lymphocyte count	25.7	
36		Mean cell volume	95.6	
37	04-MAR-2016	Mean cell volume	94.6	
38	04-MAR-2016	Monocyte count	9.9	
39	04-MAR-2016	Neutrophil count	61.5	
40		Platelet count	267000	
41	04-MAR-2016	Platelet count	219000	
42	02-MAR-2016	Proctoscopy	polyp of the sigmoid colon	
43		Protein total	14.3	
44		Protein total	6.5	
45		Protein total	17.4	
46		Protein total	14.7	
47		Protein total	6.4	
48		Prothrombin time	85 %	
49		Red blood cell count	3380000	
50	04-MAR-2016	Red blood cell count	3120000	
51		Red blood cell sedimentation rate	83	
52	27-FEB-2016	Ultrasound abdomen	Acalculous gallbladder and bile ducts explorable	
53		White blood cell count	8020	
54	04-MAR-2016	White blood cell count	7580	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low

13. Relevant Tests

Physical examination: arrhythmic cardiac action, tachycardia. Chest: vesicular murmur extensively reduced. Abdomen treatable, peristalsis present. Absent lower extremity edema
ECG (28Feb2016): AF tachycardic, signs of SVS /ischemia already known
Abdomen ultrasound (27Feb2016): test performed in Emergency/urgency and restricted due to intestinal meteorism. Acalculous gallbladder and bile ducts explorable, not dilated. Kidneys reduced in size and with cysts absent signs of bilateral hydronephrosis. Adbominal aort atheromatous, normal caliber in explorable tracts. Not effusion in the peritoneal recesses slope.
Abdomen x-ray (27Feb2016): Not significant hydrogas levels neither signs of pneumoperitoneus. Catheter for peritoneal dyalisys in left iliac fossa. vascular calcifactions diffuse.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to 1965	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
1988 to Unknown	Relevant Med History recovered	Transient ischemic attack (Transient ischaemic attack);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
1988 to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
1988 to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
2006 to Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History hospitalized from 27Feb2016 to 04Mar2016	Rectal bleeding (Rectal haemorrhage);
Unknown	Relevant Med History	Chronic renal failure (Chronic kidney disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE		Unk		70 Years	Female	88.00 kg	05	JUL	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Acute coronary infarction [Acute myocardial infarction]
thromboembolic events [Embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer non-interventional study, protocol

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 05-JUL-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) PARICALCITOL (PARICALCITOL) ; DEC-2013 / 05-JUL-2015
#2) AMLODIPINE (AMLODIPINE) ; DEC-2013 / 05-JUL-2015

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hearing impaired (Hypoacusis)
Unknown	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016295847

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-JUN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2016295847

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

EPOE-09-11, regarding subject GR-013-002. This subject of unknown gender, age and ethnicity started to receive epoetin zeta, solution for injection, dose and start date unspecified, for nephrogenic anemia. The subject's medical history and concomitant medications were not reported. On an unspecified date, the subject experienced "thromboembolic events" and, on 05Jul2015, the subject died due to acute coronary infarction. No tests or treatment were reported. The outcome of the thromboembolitic events and the status of the study drug at the time of the subject's death were unknown. On 05Jul2015, the subject had an "unscheduled-month time point". No causality assessment was provided.

Follow-up (14Jun2016): This is a follow-up report from a Pfizer non-interventional study, protocol EPOE-09-11, regarding subject GR-013-002. New information includes: The 70-years-old female subject (not pregnant) experienced Acute coronary infarctionon 05Jul2015 and passed away with date of death 05Jul2015. The patient had no known drug hypersensitivities or any history of drug dependency. Relevant medical history included sensoneural hearing impair, hyperparathyroidism, proteinuria (approximately 4 gr/24h), diabetes mellitus and hypertension. Concomitant medications included paricalcitol (PARICALCITOL) IV from Dec2013 to 05Jul2015 at 1 microcg/HD, 3 times per week for secondary hyperparathyroidism and amlodipine (AMLODIPINE) from Dec2013 to 05Jul2015 at 10 mg, 1x2 for hypertension. Laboratory examination on an unspecified date included creatinine 2.9 mg/dl and urea 80 mg/dl. Age of manifestation: 36. Family history: consanguinity. Unclear inheritance. The investigator considered that the event was not related to epoetin zeta.

Case Comment: Based on the information currently available, The Company considered there was not a reasonable possibility that the reported events Acute coronary infarction with fatal outcome and thromboembolic events were related to the study drug EPOETIN ZETA. There is limited information to this case and additional information including temporal relationship and detailed clinical course is required to better assess the case.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood creatinine	2.9 mg/dl	
2		Blood urea	80 mg/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History approximately 4 g/24h	Proteinuria (Proteinuria);
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	BULGARIA	06	MAY	1938	78 Years	Female	74.00 kg	30	JUL	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a report from a Non-interventional study, protocol EPOE-09-11, regarding subject Bg-004-0041. This 78-year-old Caucasian female subject started taking epoetin zeta 2000 (units unspecified) twice a week subcutaneously, from Mar2014 to 29Jul2016, for renal anemia. Medical history included hyperlipidemia, diabetes mellitus and hypertension.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 06-AUG-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK UNK, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) MAR-2014 / 29-JUL-2016

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CHLOPHAZOLIN (CLONIDINE HYDROCHLORIDE) ; Unknown / 30-JUL-2016
#2) FURANTHRIL /00032601/ (FUROSEMIDE) ; 30-JUL-2016 / 06-AUG-2016
#3) APIDRA (INSULIN GLULISINE) ; Unknown / 30-JUL-2016
#4) LANTUS (INSULIN GLARGINE) ; Unknown / 30-JUL-2016
#5) MOLSIDOMIN (MOLSIDOMINE) ; Unknown / 30-JUL-2016

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016403477

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-AUG-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Concomitant medications included clonidine hydrochloride (CHLOPHAZOLIN) twice a day from an unspecified date to 30Jul2016 for hypertension, furosemide (FURANTRIL) 40 mg twice a day from 30Jul2016 to 06Aug2016, insulin (APIDRA) 4 IU once a day and insulin glargine (LANTUS) 32 IU once a day both from an unspecified date to 30Jul2016 for diabetes mellitus, and molsidomin twice a day from an unspecified date to 30Jul2016. On 30Jul2016, the subject was admitted to the hospital with complaints of heaviness and pain in the chest, with irradiation to the back, and upside shortness of breath while lying down (was unable to lie). It was reported that the subject was also exposed to another erythropoietin stimulating agent epoetin beta (NEORECORMON) 81 IU weekly from Apr2013 to Mar2014. Test data, taken on unspecified dates, included activated partial thromboplastin time that was not coagulated, 89 seconds, 74.6 seconds, 46.5 seconds, 40.1 seconds, and 31.6 seconds; alanine aminotransferase of 37 IU/l; aspartate aminotransferase of 79 IU/l; base excess of -9.6, -8.1, -3.1, -3.8, -4.0, -1.6, and -0.5; chloride of 107 mmol/l, 101 mmol/l, 98 mmol/l, 102 mmol/l and 100 mmol/l; cholesterol of 6.4 mmol/l and 6.0 mmol/l; creatine phosphokinase of 261 IU/l and 703 IU/l; creatine phosphokinase MB of 30.1 ng/ml and 158.4 ng/ml; creatinine of 437 mmol/l, 439 mmol/l, 558 mmol/l, 587 mmol/l, 579 mmol/l and 537 mmol/l; glucose 8.8 mmol/l, 5.9 mmol/l, 7.7 mmol/l, 7.9 mmol/l, 7.1 mmol/l, 7.0 mmol/l, 8.5 mmol/l, 7.6 mmol/l, 6.9 mmol/l, 7.6 mmol/l, 6.0 mmol/l, 8.0 mmol/l, 6.5 mmol/l, 6.6 mmol/l and 6.7 mmol/l; potassium of 5.29 mmol/l, 5.94 mmol/l, 4.45 mmol/l, 3.74 mmol/l and 4.78 mmol/l; sodium of 138 mmol/l, 135 mmol/l, 139 mmol/l, and 138 mmol/l; triglycerides of 1.1 mmol/l and 1.5 mmol/l; urea of 24.2 mmol/l; carbon dioxide (TCO2) of 20.7, 23.8, 24.3, 24.3, 22.9, 25.2, and 26.3; hematocrit of 0.34 and 0.34; hemoglobin of 109 g/l and 112 g/l; bicarbonate (HCO3) of -19.2, 21.9, 23.0, 22.9, 21.6, 23.9 and 25.0; high density lipoprotein (HDL) of 1.73 mmol/l and 1.64 mmol/l; international normalized ratio (INR) of 1.50, 1.38 and 1.83; low density lipoprotein (LDL) of 4.1 mmol/l and 3.6 mmol/l; mean cell hemoglobin of 30.6 and 32; mean cell hemoglobin concentration (MCHC) of 321 g/l and 328 g/l; mean cell volume (MCV) of 95.4 and 95.4; saturation of 92.8, 84.7, 80.3, 90.5, 95.8, 87.6 and 94.1; partial carbon dioxide (pCO2) of 51.0, 62.5, 43.2, 46.0, 40, 41.8 and 42.5; pH of 7.18, 7.15, 7.33, 7.30, 7.341, 7.36 and 7.37; thrombocytes of 233 g/l, 249 g/l; partial oxygen (pO2) of 68, 62, 58, 64, 89, 57, and 74; prothrombin time of 66%, 73% and 55%; erythrocytes of 3.57 x10 12/l and 3.50 x10 12/l; straw blood cell (SBC) count of 17.1, 18.1, 22.3, 21.9, 21.5, 23.6 and 24.4; troponin of 1.31 ng/ml, 14.33 ng/ml, 94.32 ng/ml and 5.40 ng/ml; white blood cell count (WBC) of 14x10 9/l and 10.4x10 9/l; BEb of - 9.6, -3.1, -3.8, -4.0, -1.6 and -0.5; SBC of 17.1, 18.1, 22.3, 21.9, 21.5, 23.6, and 24.4; saturation of 84.7, 90.5, 95.8, 87.6, 94.1, and 92.8; an x-ray that showed pulmonary edema; and an echocardiography that showed mild to moderate mitral insufficiency; aortic valve without pathological lesions; without pericardial effusion. The subject was treated with furosemide (FURANTRIL), heparin, morphine 2 mg, methylprednisolone (URBASON) 20 mg, nitronal 2ml/h, acetylsalicylic acid (ASPIRIN) 1 tablet, torasemide (TRIFAS), sodium bicarbonate, dopamine, atorvastatin calcium (SORTIS) 40 mg, aceclofenac (ZOFEN) 7.5 mg, amiodarone (CORDARONE), digoxin, enoxaparin (CLEXANE), ringer, bisoprolol 5 mg, famotidine (QUATAMEL) and acenocoumarol (SINTROM). The subject had positive markers of myocardial necrosis which required emergency cardiac catheterization. Persistent significant stenosis of left anterior descending (LAD) under passable stent in the middle segment. Protracted pulmonary congestion, imposed a combination of high doses of loop diuretics. The subject was hemodynamically stabilized and moved to intensive care during day six of hospitalization. On day seven, the subject experienced hemodynamic collapse, deploy pulmonary congestion. Cardiac resuscitation was done and was not effective. On 06Aug2016 at 14:05 the subject died. The cause of death was reported as myocardial infarction. There were no risk factors for thromboembolic events or any other risk factors. The investigator considered that causal relationship to epoetin zeta was unlikely. The causality to the concomitant drugs and to the clinical trial procedure was not provided.

Case Comment: The Company considers there is a reasonable possibility that the reported myocardial infarction is related to epoetin zeta based on the known safety profile of the product. In addition, underlying hyperlipidemia, diabetes mellitus and hypertension are significant risk factors in causing the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Activated partial thromboplastin time	89 seconds	
2		Activated partial thromboplastin time	40.1 seconds	
3		Activated partial thromboplastin time	not coagulated seconds	
4		Activated partial thromboplastin time	31.6 seconds	
5		Activated partial thromboplastin time	74.6 seconds	
6		Activated partial thromboplastin time	46.5 seconds	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7		Alanine aminotransferase	37 IU/l	
8		Aspartate aminotransferase	79 IU/l	
9		Base excess	-3.1	
10		Base excess	-3.8	
11		Base excess	-0.5	
12		Base excess	-4.0	
13		Base excess	-1.6	
14		Base excess	-8.1	
15		Base excess	-9.6	
16		Blood bicarbonate	21.9	
17		Blood bicarbonate	22.9	
18		Blood bicarbonate	21.6	
19		Blood bicarbonate	19.2	
20		Blood bicarbonate	23.0	
21		Blood bicarbonate	23.9	
22		Blood bicarbonate	25.0	
23		Blood chloride	101 mmol/l	
24		Blood chloride	107 mmol/l	
25		Blood chloride	102 mmol/l	
26		Blood chloride	98 mmol/l	
27		Blood chloride	100 mmol/l	
28		Blood cholesterol	6.0 mmol/l	
29		Blood cholesterol	6.4 mmol/l	
30		Blood creatine phosphokinase	703 IU/l	
31		Blood creatine phosphokinase	261 IU/l	
32		Blood creatine phosphokinase MB	30.1 ng/ml	

Mfr. Control Number: 2016403477

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33		Blood creatine phosphokinase MB	158.4 ng/ml	
34		Blood creatinine	537 mmol/l	
35		Blood creatinine	437 mmol/l	
36		Blood creatinine	439 mmol/l	
37		Blood creatinine	558 mmol/l	
38		Blood creatinine	579 mmol/l	
39		Blood creatinine	587 mmol/l	
40		Blood glucose	6.9 mmol/l	
41		Blood glucose	7.6 mmol/l	
42		Blood glucose	7.6 mmol/l	
43		Blood glucose	8.0 mmol/l	
44		Blood glucose	8.5 mmol/l	
45		Blood glucose	7.0 mmol/l	
46		Blood glucose	7.1 mmol/l	
47		Blood glucose	7.9 mmol/l	
48		Blood glucose	7.7 mmol/l	
49		Blood glucose	5.9 mmol/l	
50		Blood glucose	8.8 mmol/l	
51		Blood glucose	6.0 mmol/l	
52		Blood glucose	6.5 mmol/l	
53		Blood glucose	6.6 mmol/l	
54		Blood glucose	6.7 mmol/l	
55		Blood potassium	5.94 mmol/l	
56		Blood potassium	5.29 mmol/l	
57		Blood potassium	4.78 mmol/l	
58		Blood potassium	3.74 mmol/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
59		Blood potassium	4.45 mmol/l	
60		Blood sodium	138 mmol/l	
61		Blood sodium	139 mmol/l	
62		Blood sodium	139 mmol/l	
63		Blood sodium	138 mmol/l	
64		Blood sodium	135 mmol/l	
65		Blood triglycerides	1.1 mmol/l	
66		Blood triglycerides	1.5 mmol/l	
67		Blood urea	24.2 mmol/l	
68		Carbon dioxide	22.9	
69		Carbon dioxide	24.3	
70		Carbon dioxide	20.7	
71		Carbon dioxide	26.3	
72		Carbon dioxide	24.3	
73		Carbon dioxide	25.2	
74		Carbon dioxide	23.8	
75		Echocardiogram	mild to moderate mitral insufficiency	
76		Haematocrit	0.34	
77		Haematocrit	0.34	
78		Haemoglobin	112 g/l	
79		Haemoglobin	109 g/l	
80		High density lipoprotein	1.73 mmol/l	
81		High density lipoprotein	1.64 mmol/l	
82		High density lipoprotein	mmol/l	
83		International normalised ratio	1.83	
84		International normalised ratio	1.50	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
85		International normalised ratio	1.38	
86		Low density lipoprotein	4.1 mmol/l	
87		Low density lipoprotein	3.6 mmol/l	
88		Mean cell haemoglobin	32	
89		Mean cell haemoglobin	30.6	
90		Mean cell haemoglobin concentration	321 g/l	
91		Mean cell haemoglobin concentration	328 g/l	
92		Mean cell volume	95.4	
93		Mean cell volume	95.4	
94		Oxygen saturation	94.1	
95		Oxygen saturation	92.8	
96		Oxygen saturation	84.7	
97		Oxygen saturation	95.8	
98		Oxygen saturation	80.3	
99		Oxygen saturation	87.6	
100		Oxygen saturation	90.5	
101		PCO2	62.5	
102		PCO2	51.0	
103		PCO2	43.2	
104		PCO2	41.8	
105		PCO2	40	
106		PCO2	46.0	
107		PCO2	42.5	
108		PO2	68	
109		PO2	57	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
110		PO2	74	
111		PO2	62	
112		PO2	58	
113		PO2	64	
114		PO2	89	
115		Platelet count	233 g/l	
116		Platelet count	249 g/l	
117		Prothrombin time	73 %	
118		Prothrombin time	66 %	
119		Prothrombin time	55 %	
120		Red blood cell abnormality	3.50 x10 12/l	
121		Red blood cell abnormality	3.57 x10 12/l	
122		Troponin	1.31 ng/ml	
123		Troponin	5.40 ng/ml	
124		Troponin	14.33 ng/ml	
125		Troponin	94.32 ng/ml	
126		White blood cell count	10.4 x10 9/l	
127		White blood cell count	14 x10 9/l	
128		X-ray	pulmonary edema	
129		pH body fluid	7.30	
130		pH body fluid	7.15	
131		pH body fluid	7.37	
132		pH body fluid	7.36	
133		pH body fluid	7.341	
134		pH body fluid	7.33	
135		pH body fluid	7.18	

ADDITIONAL INFORMATION

13. Relevant Tests

BEb (Unknown dates): -9.6, -3.1, -3.8, -4.0, -1.6, and -0.5
SBC (Unknown dates): 17.1, 18.1, 22.3, 21.9, 21.5, 23.6, and 24.4
saturation (Unknown dates): 84.7, 90.5, 95.8, 87.6, 94.1, and 92.8
echocardiography (UNKNOWN dates): mild to moderate mitral insufficiency; aortic valve without pathological lesions; without pericardial effusion

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	04	MAY	1940	76 Years	Male	85.00 kg	03	JUN	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiac infaction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study, Protocol EPOE-09-11, regarding subject 110023.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 07-JUN-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 18000 IU, (6000 IUx3 per week)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 27-MAY-2011 / 04-JUN-2016

19. THERAPY DURATION
#1) 1836 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACETYLCYSTEIN (ACETYLCYSTEINE) Effervescent tablet ; Unknown
#2) RENVELA (SEVELAMER CARBONATE) Film-coated tablet ; Ongoing
#3) MOVICOL (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BIC
#4) PREDNISOLON PFIZER (PREDNISOLONE) Tablet ; 01-JUN-2016 / Ongoing
#5) ALLOPURINOL NORDIC DRUGS (ALLOPURINOL) Tablet ; Ongoing
#6) BUFOMIX (BUDESONIDE, FORMOTEROL FUMARATE) Inhalation powder ; Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
04-MAY-2011 to 27-MAY-2011	Past Drug Event	Eprex (EPREX)
Unknown to Ongoing	Relevant Med History	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016443936

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-NOV-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 76-year-old Caucasian male patient started to receive Epoetin Zeta on 27May2011 18000 IU subcutaneously weekly at 6000 IU three times a week for renal anemia. Doses applied within the period of 3 months prior to the event included: Mean dose 1: 6000 IU three times per week. Hemoglobin: 85 g/L. Mean dose 2: 6000 IU three times per week. Hemoglobin: 94 g/L. No dose change: Dose on 07Apr2016 was 6000 IU three times per week. Hemoglobin 90 g/L. Hemoglobin on 04Jun2016: 86 g/L. The patient previously received Epoetin alfa (EPREX) 4000 IU twice a week for 7.8-8.4 g/dL from 04May2011 until 27May2011. The patient had no hyperlipidemia, ischemic heart disease, transient ischemic attack, peripheral arterial disease, diabetes mellitus, cancer, chronic gastrointestinal disease or diarrhea. There was ongoing hypertension since many years and atrial fibrillation. Additional medical history included chronic obstructive lung disease, left heart failure, combined mitral vitium, mitral insufficiency, total atrioventricular block, unspecified atrial flutter, and chronic renal failure, all ongoing, and non-rheumatic mitral stenosis. Risk factors for thrombosis events included obesity since 2011 with a body mass index (BMI) of 30 on 05Jun2015. He was a non smoker, with no recent surgery or trauma. There was no significant and short term weight changes due to fluid retention/excretion. No vascular anomalies, aneurysm, immobilization or positive family history. Other risk factors were not assessed. Concomitant medications included sevelamer carbonate (RENVELA) film coated tablet 1600 mg three times daily, prednisolone (PREDNISOLON PFIZER) tablet 30 mg every 3 days in decreasing dose since 01Jun2016, allopurinol (ALLOPURINOL NORDIC DRUGS) tablet 300 mg (200 + 100 mg) daily, budesonide/ formoterol fumarate (BUFOMIOX) inhalation powder 320/9 ug inhaled twice daily, fluticasone furoate/ vilanterol trifenatate (RELVAR ELLIPTA) inhalation powder184/22 ug inhaled once daily since 23May2016, furosemide (FURIX) tablet 250 mg once daily, metoprolol tartrate (METORPOLOL SANDOZ) modified-release tablet 150 mg once daily, ramipril (RAMIPRIL HEXAL) tablet 5 mg once daily, tolterodine L-tartrate (TOLTERODINE SANDOZ) modified release hard capsule 4 mg once daily, terazosin hydrochloride (SINALFA) tablet 5 mg once daily, finasteride (FINASTERIDE SANDOZ) film-coated tablet 5 mg once daily, omeprazole (OMEPRAZOLE TEVA) modified-release hard capsule 20 mg once daily, alfacalcidol (ETALPHA) soft capsule 0.25 ug once daily, calcium carbonate (KALCIDON) chewable tablet 500 mg once daily, calcium carbonate/ colecalciferol (KALCIPOS D3) 500 mg twice daily, and dalteparin sodium (FRAGMIN) 2500 IU once daily, all ongoing, acetylcysteine effervescent tablet 200 mg three times daily, and macrogol 3350/ potassium chloride/ sodium bicarbonate/ sodium chloride (MOVICOL) as needed. The patient experienced cardiac infarction on 03Jun2016, considered serious for life threatening, hospitalization, and fatal. Medical records from 07Jun2016 covering a time period from 03Jun2016 07Jun2016 reported that diagnoses included acute myocardial infarction, unspecified; mitral insufficiency; non rheumatic mitral stenosis, left heart failure, atrioventricular block totally, atrial fibrillation, atrial flutter unspecified, and chronic renal failure unspecified. The patient underwent doppler echocardiography, transtoracal simple, extern transtoracal pacemaker treatment, and temporary use of transvenous or epicardial pacemaker. Tests on 02Jun2016 included creatinine 903 ug/l (normal range <100), glucose 8.4 mmol/l (4-6), potassium 2.5 mmol/l (3.5-4.6) with life hemolysis in sample, sodium 135 mmol/l (137-145), C-reactive protein (CRP) 92 mg/l (<3), Hematocrit (EVF) 0.29 (0.39-0.59), hemoglobin 94 g/l (134-170), mean cell hemoglobin (MCH) 30 pg (27-33), mean cell volume (MCV) 94 fL (82-98), thrombocyte 303 x10^9/l (145-348), erythrocyte 3.1 x10^12/l (4.2-5.7), leucocyte 7.1 x10^9/l (3.5-8.8); on 03Jun2016 included albumin 22 g/l (34-45), creatinine 973 umol/l, potassium 3.9 mmol/l, sodium 138 mmol/l, CRP 78 mg/l, EVF 0.28, Hemoglobin 87 g/l, MCH 30 pg, MCV 94 fL, thrombocyte 280 x10^9/l, erythrocyte 2.9 x10^12/l (4.2-5.7), troponin T 705 ng/L at 12:04pm, 836 ng/L at 04:21pm, and 982 ng/L at 07:15pm(<15), leucocyte 10.3 x10^9/l; on 04Jun2016 included albumin 21 g/l, calcium 2.42 mmol/l (2.15-2.5), creatinine 911 ug/L, glucose 5.7 mmol/l, phosphate 2.1mmol/l (4-6), phosphate 2.1 mmol/l (0.75-1.4), potassium 4.2 mmol/l (3.5-4.6), cystatin C 8.82 mg/l (0.75-1.44), EVF 0.27, hemoglobin 86 g/l, MCH 29 pg, MCV 94 fL, thrombocyte 288 x10^9/l, erythrocyte 2.9 x10^12/l, leucocyte 9.8 x10^9/l; and on 07Jun2016 included hemoglobin 85 g/l. In summary, this was a male with renal failure on the basis of IgA-nephritis, therefore peritoneal dialysis since 12May2015, COPD, atrial fibrillation, dalteparin (FRAGMIN) as blood thinners, mild heart failure, combined mitralis vitium, and hypertension. Initially searched on 02Jun2016 and admitted to the kidney clinic due to dyspnea. Due to chest pain, moved to "us" on 03Jun2016. Care course included that interpreted as Non-ST Segment Elevation Myocardial Infarction (NSTEMI). He received conservative treatment deciding on no cardiac lung rescue. Due to anemia, blood transfusions were given. The night to 07Jun2016, again episodes of pressure over the chest affected by self-terminating asystole and then bradycardia with ventricular rate about 26/min. He was moved to the heart intensive clinic. He expressed wishes that they should do what they can if he got a cardiac arrest but did not want to be a "package". Affected by repeated asystoles/pronounced bradycardia in the heart intensive clinic, cardiac lung rescue performed several times, repeating epinephrine (ADRENALIN) injections reproduced palpable pulse every time. A decision was made for temporary pacemaker and coronary angiography. He was moved to the angio laboratory. Even there, he was repeating asystoles. External pacing with hesitant effect, epinephrine workes continuing. Finally, the patient was affected by pulseless electrical activity (PEA). Bedside echo show almost stagnated left-ventricular. Further resuscitation measures assessed as not defensible considering the patient's desire and with thought of risk of remaining nerurological sequelae, there was also unlikely that the left- ventricle should get back any pump capacity to speak about. Assessment was probably NSTEMI which has caused an over line disturbances and then even pump failure. The patient died on 07Jun2016. The cause of death was cardiac infarction, which was determined by autopsy. Treatments given after on or after date of event included mepivacaine hydrochloride (CARBOCAIN) 10mg/ml started on 07Jun2016, acetylsalicylic acid (BAMYL) 500mg on 03Jun2016, acetylsalicylic acid (TROMBYL) 75 mg started 03Jun2016 sodium polystyrene sulfonate (RESONIUM) 450g on 03Jun2016, atropine 0.5mg/ml given 3 times on 07Jun2016, Erytrocyte concentration given 06Jun2016 and 07Jun2016, heparin 5000 iu/ml given on 07Jun2016, epinephrine (ADRENALINE) 10ml 0.1 mg/ml given 3 times on 07Jun2016, Physioneal and Extraneal (periotonal dialysis) given from 03Jun2016, and Isosorbide mononitrate (IMDURAL) 30mg started on 04Jun2016. Epoetin zeta was permanently withdrawn on 04Jun2016. The event was assessed as unlikely related to study product. The patient had at first been hospitalized in another hospital.

Follow-up (06Oct2016): New information received from the investigator included: death and autopsy details.

Follow-up (18Nov2016): New information received from the investigator included: Subject ID corrected to 110023.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Case Comment: In Agreement with the investigator's assessment, the Company considered there was not a reasonable possibility that the reported Cardiac infaction was related to EPOETIN ZETA. The event was most likely related to an intercurrent or underlying condition. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	03-JUN-2016	Blood albumin	22 g/l	45 34
2	04-JUN-2016	Blood albumin	21 g/l	45 34
3	04-JUN-2016	Blood calcium	2.42 mmol/l	2.50 2.15
4	02-JUN-2016	Blood creatinine	903 ug/L	<100
5	03-JUN-2016	Blood creatinine	973 ug/L	<100
6	04-JUN-2016	Blood creatinine	911 ug/L	<100
7	02-JUN-2016	Blood glucose	8.1 mmol/l	6.0 4.0
8	04-JUN-2016	Blood glucose	5.7 mmol/l	6.0 4.0
9	04-JUN-2016	Blood phosphorus	2.1 mmol/l	1.4 0.75
10	02-JUN-2016	Blood potassium	5.8 mmol/l	4.6 3.5
11	03-JUN-2016	Blood potassium	3.9 mmol/l	4.6 3.5
12	04-JUN-2016	Blood potassium	4.2 mmol/l	4.6 3.5
13	02-JUN-2016	Blood sodium	135 mmol/l	145 137
14	03-JUN-2016	Blood sodium	138 mmol/l	145 137
15	02-JUN-2016	C-reactive protein	92 mg/l	<3
16	03-JUN-2016	C-reactive protein	78 mg/l	<3
17	04-JUN-2016	Cystatin C	8.82 mg/l	1.44 0.75
18	02-JUN-2016	Haematocrit	0.29	0.59 0.39
19	03-JUN-2016	Haematocrit	0.28	0.59 0.39
20	04-JUN-2016	Haematocrit	0.27	0.59 0.39
21	02-JUN-2016	Haemoglobin	94 g/l	170 134
22	03-JUN-2016	Haemoglobin	87 g/l	170 134
23	04-JUN-2016	Haemoglobin	86 g/l	170 134
24	07-JUN-2016	Haemoglobin	85 g/l	170 134

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
25	02-JUN-2016	Mean cell haemoglobin	30 pg	33 27
26	03-JUN-2016	Mean cell haemoglobin	30 pg	33 27
27	04-JUN-2016	Mean cell haemoglobin	29 pg	33 27
28	02-JUN-2016	Mean cell volume	94 fL	98 82
29	03-JUN-2016	Mean cell volume	94 fL	98 82
30	04-JUN-2016	Mean cell volume	94 fL	98 82
31	02-JUN-2016	Platelet count	303 x10 9/l	348 145
32	03-JUN-2016	Platelet count	280 x10 9/l	348 145
33	04-JUN-2016	Platelet count	288 x10 9/l	348 145
34	02-JUN-2016	Red blood cell count	3.1 x10 12/l	5.7 4.2
35	03-JUN-2016	Red blood cell count	2.9 x10 12/l	5.7 4.2
36	04-JUN-2016	Red blood cell count	2.9 x10 12/l	5.7 4.2
37	03-JUN-2016	Troponin T	836 ng/L	<15
38	03-JUN-2016	Troponin T	705 ng/L	<15
39	03-JUN-2016	Troponin T	982 ng/L	<15
40	02-JUN-2016	White blood cell count	7.1 x10 9/l	8.8 3.5
41	03-JUN-2016	White blood cell count	10.3 x10 9/l	8.8 3.5
42	04-JUN-2016	White blood cell count	9.8 x10 9/l	8.8 3.5

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) MOVICOL (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE) ; Unknown

#7) RELVAR ELLIPTA (FLUTICASONE FUROATE, VILANTEROL TRIFENATATE) Inhalation powder ; 23-MAY-2016 / Ongoing

#8) FURIX (FUROSEMIDE) Tablet ; Ongoing

#9) METOPROLOL SANDOZ (METOPROLOL TARTRATE) Modified-release tablet ; Ongoing

#10) RAMIPRIL HEXAL (RAMIPRIL) Tablet ; Ongoing

#11) TOLTERODINE SANDOZ (TOLTERODINE L-TARTRATE) Modified-release capsule, hard ; Ongoing

#12) SINALFA (TERAZOSIN HYDROCHLORIDE) Tablet ; Ongoing

#13) FINASTERIDE SANDOZ (FINASTERIDE) Film-coated tablet ; Ongoing

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#14) OMEPRAZOLE TEVA (OMEPRAZOLE) Modified-release capsule, hard ; Ongoing

#15) ETALPHA (ALFACALCIDOL) Capsule, soft ; Ongoing

#16) KALCIDON (CALCIUM CARBONATE) Chewable tablet ; Ongoing

#17) KALCIPOS D3 (CALCIUM CARBONATE, COLECALCIFEROL) Film-coated tablet ; Ongoing

#18) FRAGMIN (DALTEPARIN SODIUM) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Chronic obstructive lung disease (Chronic obstructive pulmonary disease);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Left heart failure (Left ventricular failure);
Unknown to Ongoing	Relevant Med History	Mitral valve disease (Mitral valve disease);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Mitral insufficiency (Mitral valve incompetence);
Unknown	Relevant Med History	Mitral stenosis (Mitral valve stenosis);
Unknown to Ongoing	Relevant Med History	Atrioventricular block complete (Atrioventricular block complete);
Unknown to Ongoing	Relevant Med History	Atrial flutter (Atrial flutter);
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease);
2011 to Unknown	Relevant Med History BMI 30	Obesity (Obesity);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	28	JUN	1936	80 Years	Male	81.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart attack [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a non-Interventional study report from the observational study protocol EPOE-09-11, regarding subject 4710016.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 19-SEP-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 and 3000 IU in change

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) JUN-2014 / MAY-2016

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) VALSARTAN HEXAL (VALSARTAN) ; Unknown
#2) METOPROLOL RETARD HEUMANN (METOPROLOL) ; Unknown
#3) ASS CT (ACETYLSALICYLIC ACID) ; Unknown
#4) SIMVABETA (SIMVASTATIN) Tablet ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Smoker (Tobacco user)
	5-10 cigarettes / day	
Unknown	Relevant Med History	Atherosclerosis generalized (Arteriosclerosis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016459865

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JAN-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 80-year-old Caucasian male subject received epoetin zeta (RETACRIT) 2000 and 3000 IU "in change" from Jun2014 to May2016 then 3000 IU from May2016 to Sep2016 for the study indication of renal anemia. There were no dose changes within the 3 months prior to the event. The last dose prior to the event was administered on 16Sep2016. At no time was the subject exposed to any other erythropoietin stimulating agent (ESA) or experience any other thromboembolitic event during treatment with any other ESA. His medical history was significant for generalized atherosclerosis, a transient ischemic attack (TIA), peripheral artery disease (PAD), and hypertension. The subject smoked 5-10 cigarettes per day, but did not suffer from any of the following risk factors for thromboembolic events: adipositas, factor V Leiden, protein C or S deficiency, antithrombin III deficiency, prothrombin G20210A mutation, homocysteine anemia, recent surgeries, trauma, immobilization or positive family history. Furthermore, the subject did not suffer from hyperlipidemia, diabetes mellitus, cancer nor any chronic gastrointestinal disorders. His concomitant medications included valsartan (VALSARTAN HEXAL) 80 mg, metoprolol (METOPROLOL RETARD HEUMANN) 100 (units not provided), acetylsalicylic acid (ASS CT) 1 dosage form and simvastatin (SIMVABETA) 30 mg tablet, all taken by mouth daily. On an unspecified date, the subject suffered a heart attack and died on 19Sep2016. The event was also considered life-threatening. No autopsy was performed. It was reported the subject had hemodialysis but was not hospitalized due to the heart attack. Tests included partial thromboplastin time (PTT) 41 seconds (range: 26 to 40) on 22Aug2016, alanine aminotransferase (ALAT) 0.16 umol/l (0.17 to 0.83) on 25Jul2016, calcium 2.08 mmol/l (2.20 to 2.55) on 25Jul2016 and 1.97 on 22Aug2016, creatinine 673 umol/l (62 to 106) on 25Jul2016 and 649 umol on 22Aug2016, iron 4.56 umol/l (7.2 to 21.5) on 06Jun2016 and 6.27 umol/l on 22Aug2016, phosphorus 2.16 mmol/l (0.87 to 1.45) on 25Jul2016 and 2.26 mmol/l on 22Aug2016, potassium 5.4 mmol/l (3.5 to 5.1) on 22Aug2016, potassium 6.32 mmol/l (3.5 to 5.1 mmol/l) on 25Jul2016 and 6.33 mmol/l on 22Aug2016, sodium 145.2 mmol/l (135 to 145), urea 19.90 mmol/l (1.70 to 8.30) on 25Jul2016 and 26.80 mmol/l on 22Aug2016, uric acid 501 umol/l (202 to 416) on 06Jun2016, gamma-GT 1.22 umol/l (0.17 to 1.19) on 22Aug2016, glomerular filtration rate 10.2 ml/min (60-89) on 22Aug2016, hematocrit 38.1% (41 to 53) on 22Aug2016 and 38.8% on 05Sep2016, hemoglobin 7.8 mmol/l (8.10 to 11.2) on 22Aug2016 and 8.0 mmol/l on 05Sep2016, erythrocytes 4.00 x10 3/mm3 (4.5 to 5.9) on 22Aug2016 and 4.25 x10 3/mm3 on 05Sep2016, transferrin 1.6 g/l (2.0 to 3.6) and 1.4 g/l on 22Aug2016, transferrin saturation 11.1% (16 to 45) on 22Aug2016, and leukocytes 11.23 (3.7 to 9.9) on an unknown date, 10.83 on 22Aug2016 and 11.13 on 05Sep2016. It was reported that there was no data available regarding reticulocytes, C-reactive protein, blood sedimentation rate, ECG, echocardiography, Troponin I and T, creatinine kinase or angiography. The action taken with the study drug was reported as not applicable. The investigator reported that the relationship of the event to treatment with epoetin zeta was unrelated.

Follow-up (16Nov2016): Updates event term from death NOS to heart attack, causality details, test data and event details.

Follow-up (23Nov2016): Updates study drug details, concomitant medications

Follow-up (29Nov2016): Updates start and stop dates of study drug and date of death.

Follow-up (14Dec2016): Updates study drug data, risk factor information, and test data comments.

Follow-up (11Jan2017): Updates study drug details (dose and frequency).

Follow-up (17Jan2017): Updates study drug details

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event Heart attack with fatal outcome was related to the study drug. The medical history of smoking , generalized atherosclerosis, a transient ischemic attack, peripheral artery disease and hypertension may provide plausible explanations for the event. The follow up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	22-AUG-2016	Activated partial thromboplastin time prolonged	41 seconds	40 26
2	25-JUL-2016	Alanine aminotransferase	0.16 umol/l	0.83 0.17
3	25-JUL-2016	Blood calcium	2.08 mmol/l	2.55 2.20
4	22-AUG-2016	Blood calcium	1.97 mmol/l	2.55 2.20
5	25-JUL-2016	Blood creatinine	673 umol/l	106 62
6	22-AUG-2016	Blood creatinine	649 umol/l	106 62
7	06-JUN-2016	Blood iron	4.56 umol/l	21.5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				7.2
8	22-AUG-2016	Blood iron	6.27 umol/l	21.5 7.2
9	25-JUL-2016	Blood phosphorus	2.16 mmol/l	1.45 0.87
10	22-AUG-2016	Blood phosphorus	2.26 mmol/l	1.45 0.87
11	25-JUL-2016	Blood potassium	6.32 mmol/l	5.1 3.5
12	22-AUG-2016	Blood potassium	6.33 mmol/l	5.1 3.5
13	22-AUG-2016	Blood potassium	5.4 mmol/l	5.1 3.5
14	22-AUG-2016	Blood sodium	145.2 mmol/l	145 135
15	25-JUL-2016	Blood urea	19.90 mmol/l	8.30 1.70
16	22-AUG-2016	Blood urea	26.80 mmol/l	8.30 1.70
17	06-JUN-2016	Blood uric acid	501 umol/l	416 202
18	22-AUG-2016	Gamma-glutamyltransferase increased	1.22 umol/l	1.19 0.17
19	22-AUG-2016	Glomerular filtration rate	10.2 ml/min	60-89
20	22-AUG-2016	Haematocrit	38.1 %	53 41
21	05-SEP-2016	Haematocrit	38.8 %	53 41
22	22-AUG-2016	Haemoglobin	7.8 mmol/l	11.2 8.10
23	05-SEP-2016	Haemoglobin	8.0 mmol/l	11.2 8.10
24	22-AUG-2016	Red blood cell scan	4.00 x10 3/mm3	5.9 4.5
25	05-SEP-2016	Red blood cell scan	4.25 x10 3/mm3	5.9 4.5
26	06-JUN-2016	Transferrin	1.6 g/l	3.6 2.0
27	22-AUG-2016	Transferrin	1.4 g/l	3.6 2.0
28	22-AUG-2016	Transferrin saturation	11.1 %	45 16
29		White blood cell count	11.23	9.9 3.7
30	22-AUG-2016	White blood cell count	10.83	9.9 3.7
31	05-SEP-2016	White blood cell count	11.13	9.9 3.7

Mfr. Control Number: 2016459865

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	3000 IU, UNK; Intravenous	renal anemia (Nephrogenic anaemia)	MAY-2016 / SEP-2016; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	BULGARIA	08	OCT	1937	79 Years	Female	65.00 kg	15	OCT	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischemic stroke [Ischaemic stroke]

Case Description: EPOE-09-11: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non-Interventional Study for Protocol EPOE-09-11PASCO II, regarding subject BG-001-0048.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 17-OCT-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 80 IU/kg, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 03-AUG-2015 / 13-OCT-2016

19. THERAPY DURATION
#1) 438 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DOXAZOSIN MESILATE (DOXAZOSIN MESILATE) ; OCT-2016 / Unknown
#2) CORINFAR (NIFEDIPINE) ; OCT-2016 / Unknown
#3) CHLOPHAZOLIN (CLONIDINE HYDROCHLORIDE) ; OCT-2016 / Unknown
#4) CANDESARTAN (CANDESARTAN) ; OCT-2016 / Unknown
#5) ISODINIT (ISOSORBIDE DINITRATE) ; OCT-2016 / Unknown
#6) INSULIN ACTRAPID HM (INSULIN HUMAN) ; OCT-2016 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)
Unknown	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016495673

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-NOV-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 79-year-old Caucasian female subject received epoetin zeta (RETACRIT) 80 IU/kg subcutaneously two times a week from 03Aug2015 to 13Oct2016 for renal anemia. The batch was reported as GP005P6. The subject's medical history included diabetes mellitus and hypertension. There were no other risk factors reported. Concomitant medications included nifedipine (CORINFAR RETARD) 20 mg once daily, clonidine (CHLOPHAZOLIN) 4 times daily, candesartan 8mg once daily, isosorbide dinitrate (ISODINIT) 20 mg twice daily, doxazosin 16 mg 4 times daily, all since Oct2016 taken for hypertension, and insulin human (INSULIN ACTRAPID HM) twice daily taken for diabetes mellitus since Oct2016. On an unspecified date the subject was having hemodialysis. He experienced ischemic stroke and was hospitalized on 15Oct2016. The event was considered life threatening. On 15Oct2016, the following testing information was provided: blood sugar at 9.4 at 6:00h at 8.1 at 24:00 h. On 16Oct2016, the following testing information was provided: blood sugar 2 at 6.8, leukocytes (WBS (Leu)) at 18,9, eythrocytes (RBC (Er)) at 3,33, hemoglobin (Hb) at 100, hematocrit (Ht) at 0,31, thrombocytes (Tr) at 162. mean cell volume (MCV) at 93.1, mean cell hemoglobin (MCH) at 30,0, MCHC at 323, erythrocyte sedimentaiton rate (ESR) at 30, creatinine at 457, urea at 10,11, potassium at 5.75, sodium at 98, chloridy at 71, glucose in urine test stripe at 1.0, bilirubin urine test stripe negative, ketone urine test stripe negative, special gravity urine test strip at 1.02, blood in urine test strip at 2.0, pH urine test strip at 7.0, protein in the urine test strip at 3.0, urobilinogen urine test normal, nitrites in the urine negative, leucocytes urine test strip at 3.0, blood sugar at 6:00 AM at 11.8, at 12:00 PM at 9.8, at 6:00 PM at 10.7, 12:00 AM at 11,00, pH at 7.45, carbon dioxide (pCO2) at 25, oxygen (pO2) at 49, bicarbonate (HCO3) act at 17, HCO3 stat at 20, BE (cct) at -5, BE (b) at -6, O2 sat.-86, CO2 at 40, BB (buffer base). On17Oct2016, the following testing information was provided: blood sugar at 6:00-ex, 12:00-ex, 18:00-ex,24:00-ex, hematocrit at 0.32, creatinine at 648, urea at 19.82, potassium at 6.78, sodium at 137, chloridy at 101. An electrocardiogram (EKG) from an unspecified date showed sinus rhythm. Computer tomography (CT) of brain from an unspecified date showed no visual evidence of vascular, traumatic or volumetric changes in the tissues of both medullary hemisphere; there was data of parietal ischemic- bilateral parietal; expressed diffusional cortical atrophy; brain systems were normal. X-ray of chest and lung from an unspecified date showed enlightened bilateral pulmonary parenchyma, heart shadow with moderately enlarged transverse dimension. The last result of Hb from an unspecified date was 100 g/L. Treatment for the event included: mannitol 250 mg two times daily for 3 days, sodium chloride 500 ml twice daily for 3 days, chlophazoline 1 ampule (amp.) twice daily for 2 days and then changed to tablets 4 times daily for one day, enoxaparin sodium (CLEXANE) 0,6 1 flacon daily for 3 days; ACTRAPID insulin for 3 days regarded the high blood sugar; furosemide (FURANTHRIL) 1 amp. daily, sodium bicarbonate 1amp. daily, metamizole sodium (ANALGIN) amps., nifedipine (CORINFAR) 3 x 1 tablets, for 1 day, candesartan one tablet twice daily for 1 day, doxasosine, isosorbite dinitrate (ISODINIT) 3 times daily for 1 day. No action was taken with epoetin zeta in response to the event. The subject was in terminal condition, coma, muscular hypotonia, dysrhythmic superficial breathing, blood pressure was not detected and 10.05 exitus letalis. The subject died on 17Oct2016. It was unknown if an autopsy was completed. The subject was released from the autopsy at the request of her relatives. The investigator considered that there was not a reasonable possibility that the event ischemic stroke was related to the study drug.

Follow-up (01Nov2016 and 02Nov2016): Adds test data, treatment, event details, and updates study drug dosage regimen.

Case Comment: In agreement with the investigator, the Company considered that there was not a reasonable possibility that the event ischemic stroke was related to the study drug. The underlying diabetes mellitus, hypertension, renal disease and advanced age were significant risk factors for the event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	16-OCT-2016	Albumin urine	3.0	
2	16-OCT-2016	Bilirubin urine	Negative	
3	16-OCT-2016	Blood bicarbonate	17	
4	16-OCT-2016	Blood bicarbonate	20	
5	16-OCT-2016	Blood chloride	71	
6	17-OCT-2016	Blood chloride	101	
7	16-OCT-2016	Blood creatinine	457	
8	17-OCT-2016	Blood creatinine	648	
9	15-OCT-2016	Blood glucose	9.6 at 6	
10	15-OCT-2016	Blood glucose	8.1 at 24	

Mfr. Control Number: 2016495673

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
11	16-OCT-2016	Blood glucose	9.8 at 12	
12	16-OCT-2016	Blood glucose	10.7 at 18	
13	16-OCT-2016	Blood glucose	11.8 at 6	
14	16-OCT-2016	Blood glucose	11.0 at 24	
15	17-OCT-2016	Blood glucose	ex at 12	
16	17-OCT-2016	Blood glucose	ex at 24	
17	17-OCT-2016	Blood glucose	ex at 18	
18	17-OCT-2016	Blood glucose	ex at 6	
19	16-OCT-2016	Blood potassium	5.75	
20	17-OCT-2016	Blood potassium	6.78	
21	16-OCT-2016	Blood sodium	98	
22	17-OCT-2016	Blood sodium	137	
23	16-OCT-2016	Blood urea	10.11	
24	17-OCT-2016	Blood urea	19.82	
25	16-OCT-2016	Blood urine	2.0	
26	16-OCT-2016	Carbon dioxide	40	
27		Computerised tomogram head	no visual evidence of vascular, traumatic or volum	
28		Electrocardiogram	sinus rhythm	
29	16-OCT-2016	Glucose urine	1.0	
30	16-OCT-2016	Haematocrit	0.31	
31	17-OCT-2016	Haematocrit	0.32	
32		Haemoglobin	100 g/l	
33	16-OCT-2016	Haemoglobin	100 g/l	
34	16-OCT-2016	Mean cell haemoglobin	30.0	
35	16-OCT-2016	Mean cell haemoglobin concentration	323	

Mfr. Control Number: 2016495673

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
36	16-OCT-2016	Mean cell volume	93.1	
37	16-OCT-2016	Nitrite urine test tape	Negative	
38	16-OCT-2016	Oxygen saturation	86	
39	16-OCT-2016	PCO2	25	
40	16-OCT-2016	PO2	49	
41	16-OCT-2016	Platelet count	162	
42	16-OCT-2016	Red blood cell count	3.33	
43	16-OCT-2016	Red blood cell sedimentation rate	30	
44	16-OCT-2016	Specific gravity urine	1.02	
45	16-OCT-2016	Urine ketone body absent	Negative	
46	16-OCT-2016	Urobilinogen urine	Normal	
47	16-OCT-2016	White blood cell count	18.9	
48	16-OCT-2016	White blood cells urine positive	3.0	
49		X-ray	enlightened bilateral pulmonary parenchyma	
50	16-OCT-2016	pH body fluid	7.45	
51	16-OCT-2016	pH body fluid	7.0	

13. Relevant Tests

Blood glucose (15Oct2016) - 6 o'clock - 9.4; 24 o'clock - 81.
Blood glucose (16Oct2016) - 6 o'clock - 11.8; 12 o'clock - 9.8; 18 o'clock - 10.7; 24 o'clock - 11.0
HCO3 act (16Oct2016): 17
HCO3 stat (16Oct2016): 20
BE (ctf) (16Oct2016): - 5
BE (b) (16Oct2016): 6
Computer tomography (CT) of brain (unknown date): showed no visual evidence of vascular, traumatic or volumetric changes in the tissues of both medullary hemisphere; there was data of parietal ischemic- bilateral parietal; expressed diffusional cortical atrophy; brain systems normal.
X-ray of chest and lung (unknown date): enlightened bilateral pulmonary parenchyma, heart shadow with moderately enlarged transverse dimension

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	17	DEC	1935	80 Years	Male	91.00 kg	08	DEC	2016	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

decompensation chronic right heart failure and heart attack [Chronic right ventricular failure]
decompensation chronic right heart failure and heart attack [Condition aggravated]
decompensation chronic right heart failure and heart attack [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 08-DEC-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 1000 IU, 3 (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 09-DEC-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS ISIS 100 (ACETYLSALICYLIC ACID) Tablet ; 20-AUG-2010 / Unknown
#2) BERLINSULIN H NORMAL (INSULIN HUMAN) Solution for injectio
#3) BERLINSULIN H BASAL (INSULIN HUMAN INJECTION, ISOPHA
#4) PREDNISOLON JENAPHARM (PREDNISOLONE) Tablet ; 15-SEP-2015 / Unknown
#5) TORASEMID-1A PHARMA (TORASEMIDE) Tablet, 100 mg; 25-OCT-2016 / Unknown
#6) ULTIBRO (GLYCOPYRRONIUM BROMIDE, INDACATEROL MALEAT
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)
Unknown	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016583774

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-MAR-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(PASCO II)

This is a Non-Interventional Study report from the observational study, Protocol EPOE-09-11. This 80-year-old Caucasian male subject started treatment with epoetin zeta (RETACRIT) from 09Dec2014, administered intravenously at 1000 IU three times per week (Tuesday, Thursday and Saturday) for renal anemia as per study protocol. The subject reportedly received dose on 10Oct2016; the last dose before the event was given on 06Dec2016. The dose was not changed in the last three weeks prior to the event, and no other erythropoietin stimulating medications were received at any time point. The subject was on hemodialysis.
The subject's medical history included hyperlipidemia, hypertension, bladder cancer from 2014 to 2015, chronic right heart failure since approximately 2010, chronic obstructive pulmonary disease (COPD) since 2013 and chronic bronchitis since 2013. It was reported that no risk factors were known.
Concomitant medications included acetylsalicylic acid (ASS ISIS 100) 1 dosage form (DF) once daily in the morning since 20Aug2010 for coronary sclerosis, prednisolone (PREDNISOLON JENAPHARM) 5 mg once daily in the morning since 15Sep2015 for chronic obstructive bronchitis, torasemide (TORASEMID-1A PHARMA) 200 mg once daily in the morning since 25Oct2016 for kidney failure, glycopyrronium bromide/ indacaterol maleate (ULTIBRO) 85 ug/ 43 ug once daily since 05Nov2015 for COPD, acetylcysteine (ACC 600) 1 DF once daily since 12Apr2016 for bronchitis, metamizole sodium (NOVALGIN) 20 drops as needed since 10Nov2016 for bone and spine pain, calcium acetate (CALCIUM ACETATE 500) 1 DF in the morning, 2 DF at noon, and 2 DF in the evening (total of 5 DF daily) since 30Jun2016 for elevation of phosphorus in chronic kidney disease (CKD), lactulose (LACTULOSE AL) 20 ml as needed since 10Nov2016 for constipation, dimetindene maleate (FENISTIL) 1 DF twice daily in the morning and evening since 17Oct2016 for pruritus, alfacalcidol (TEVACIDOL) 1 mcg daily in the morning since 30Jun2016, sevelamer hydrochloride (RENAGEL) 800 mg twice daily in the morning and evening since 25Aug2016, sevelamer carbonate (RENVELA) 2.4 grams once daily at noon since 25Aug2016, and sodium bicarbonate (NEPHROTRANS) 1680 mg twice daily in the morning and evening since 11Nov2016, all four for chronic kidney disease (CKD), glucagon hydrochloride (GLUCAGEN HYPOKIT) at unspecified dosage subcutaneously since 18Jul2016 for diabetes mellitus, cefuroxime axetil (CEFUHEXAL 250) 1 DF twice daily in morning and evening since 06Dec2016 for bronchitis, all by mouth, insulin human (BERLINSULIN H NORMAL) 12 IU in the morning, 10 IU at noon, 10 IU in evening (total of 32 IU daily) and insulin human injection/ isophane (BERLINSULIN H BASAL) 14 IU daily once daily at night, both subcutaneously since 07Jun2013 for diabetes mellitus, and denosumab (PROLIA) 60 mg subcutaneously every six months since 07Jun2016 (previously reported as with the last dose received 06Jun2016) for osteoporosis, sodium ferric gluconate (FERRLECIT) 62.5 mg injection, 0.5 dosage form at noon on Tuesdays and Saturdays since 19Nov2016 for iron deficiency, ambroxol hydrochloride (AMBROXOL CT) 15 mg/2 ml injection, 1 DF intravenously at noon since 03Nov2015 for bronchitis, paricalcitol (PARICALCITOL RATIOPHARM) 5 ug/ml 1 DF intravenously daily at noon on Tuesdays since 28Jul2016 for CKD.
The subject experienced a heart attack and died. The date of the heart attack and date of death were reported as 08Dec2016. It was reported that the subject died in the hospital. The cause for admission was severe dyspnea following bronchitis. The subject was treated for the bronchitis since 06Dec2016 with a cephalosporine. Despite antibiotic therapy, the subject's dyspnea deteriorated, and therefore, was admitted to the hospital. The death was the result decompensation chronic right heart failure due to COPD. The event terms were reported as acute exacerbation of chronic obstructive bronchitis with onset date of 2013 (as reported), considered medically significant, and decompensation chronic right heart failure and heart attack with an onset date of 08Dec2016 and serious as due to being fatal. On 30Mar2017, the bronchitis was not considered reportable. There was no embolic event. Tests included, alkaline phosphatase (ALP) 1.4 (normal range (NR): 0.67-2.15), uric acid 594 umol/l (NR: 202-416), gamma GT (GGT) 2.27 (NR: 0.17-1.19), all on 23Aug2016; creatinine 727 umol/l (NR: 62-106), serum anorganic phosphate 1.57 mmol/l (NR: 0.87-1.45), potassium 5.07 mmol/l (NR: 3.5-5.1), urea 22.9 mmol/l (NR: 1.7-8.3), glomerular filtration rate (GFR) 9.2 ml/min (NR: 60-89), hematocrit (Hct) 34.3% (NR: 41-53), hemoglobin (Hg) 6.8 mmol/l (NR: 8.1-11.2), RBC count 3.51 x10 12/l (NR: 4.5-5.9), serum ferritin 263 ng/ml (NR: 30-400), serum transferrin 2.1 g/l (NR:2-3.6), all on 18Oct2016; and ALP 2.49, creatinine 706 umol/l, serum anorganic phosphate 1.82 mmol/l, potassium 5.15 mmol/l, urea 22.10 mmol/l, uric acid 518 umol/l, GGT 4, GFR 9.4 ml/min, Hct 31.5%, Hg 6.4 mmol/l, RBC count 3.32x10 12/l, serum ferritin 505.5 ng/ml, serum transferrin 1.8 g/l, all on 15Nov2016. In summary, decompensation chronic right heart failure and heart attack were the cause of death. The action taken with epoetin zeta in response to the event was reported as not applicable. An autopsy was not performed. The outcome of the event acute exacerbation of chronic obstructive bronchitis was unknown. The investigator reported that the event decompensation chronic right heart failure and heart attack was unrelated to treatment with the study medication, and any concomitant medications and acute exacerbation of chronic obstructive bronchitis was also unrelated to the study medication. The investigator added that a relation to the low dose treatment with epoetin zeta was unlikely.

Follow-up (16Dec2016): Updates subject's age, gender, study drug information, medical history, test data.

Follow-up (23Dec2016): Updates event start date, concomitant medications.

Follow-up (11Jan2017): Confirms event term is heart attack and clarifies HD abbreviation (hemodialysis).

Follow-up (13Jan2017): Updates reaction details, concomitant medication details.

Follow-up (13Feb2017): Adds causality assessment for clinical trial procedure, updates medical history, event details, and cause of death.

Follow-up (17Feb2017): Updates medical history and event details.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Follow-up (22Feb2017): Adds event, chronic bronchitis, updates event term from heart attack to chronic right heart failure.

Follow-up (24Feb2017): Updates event term from chronic right heart failure to decompensation chronic right heart failure, cause of death and medical history.

Follow-up (07Mar2017): Event term was updated from chronic bronchitis to acute exacerbation of chronic obstructive bronchitis

Follow-up (29Mar2017): Updates event term from decompensation chronic right heart failure to decompensation chronic right heart failure and heart attack.

Follow-up (30Mar2017): The event acute exacerbation of chronic obstructive bronchitis was deleted.

Case Comment: In agreement with the investigator's assessment, the Company considered there was not a reasonable possibility that the reported event decompensation chronic right heart failure and heart attack was unrelated to treatment with the study medication, and any concomitant medications.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	23-AUG-2016	Blood alkaline phosphatase	1.4	2.15 0.67
2	15-NOV-2016	Blood alkaline phosphatase	2.49	2.15 0.67
3	18-OCT-2016	Blood creatinine	727 umol/l	106 62
4	15-NOV-2016	Blood creatinine	706 umol/l	106 62
5	18-OCT-2016	Blood phosphorus	1.57 mmol/l	1.45 0.87
6	15-NOV-2016	Blood phosphorus	1.82 mmol/l	1.45 0.87
7	18-OCT-2016	Blood potassium	5.07 mmol/l	5.1 3.5
8	15-NOV-2016	Blood potassium	5.15 mmol/l	5.1 3.5
9	18-OCT-2016	Blood urea	22.9 mmol/l	8.3 1.7
10	15-NOV-2016	Blood urea	22.10 mmol/l	8.3 1.7
11	23-AUG-2016	Blood uric acid	594 umol/l	416 202
12	15-NOV-2016	Blood uric acid	518 umol/l	416 202
13	23-AUG-2016	Gamma-glutamyltransferase	2.27	1.19 0.17
14	15-NOV-2016	Gamma-glutamyltransferase	4	1.19 0.17
15	18-OCT-2016	Glomerular filtration rate	9.2 ml/min	89 60
16	15-NOV-2016	Glomerular filtration rate	9.4 ml/min	89 60
17	18-OCT-2016	Haematocrit	34.3 %	53 41
18	15-NOV-2016	Haematocrit	31.5 %	53 41
19	18-OCT-2016	Haemoglobin	6.8 mmol/l	11.2 8.1

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
20	15-NOV-2016	Haemoglobin	6.4 mmol/l	11.2 8.1
21	18-OCT-2016	Red blood cell count	3.51 x10 12/l	5.9 4.5
22	15-NOV-2016	Red blood cell count	3.32 x10 12/l	5.9 4.5
23	18-OCT-2016	Serum ferritin	263 ng/ml	400 30
24	15-NOV-2016	Serum ferritin	505.5 ng/ml	400 30
25	18-OCT-2016	Transferrin	2.1 g/l	3.6 2.0
26	15-NOV-2016	Transferrin	1.8 g/l	3.6 2.0

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	1000 IU, 3x per week (Tuesday, Thursday, Saturday); Intravenous	Renal anemia (Nephrogenic anaemia)	09-DEC-2014 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) BERLINSULIN H NORMAL (INSULIN HUMAN) Solution for injection in pre-filled pen ; 07-JUN-2013 / Unknown

#3) BERLINSULIN H BASAL (INSULIN HUMAN INJECTION, ISOPHANE) ; 07-JUN-2013 / Unknown

#6) ULTIBRO (GLYCOPYRRONIUM BROMIDE, INDACATEROL MALEATE) ; 05-NOV-2015 / Unknown

#7) ACC 600 TABS (ACETYLCYSTEINE) ; 12-APR-2016 / Unknown

#8) NOVALGIN (METAMIZOLE SODIUM) ; 10-NOV-2016 / Unknown

#9) CALCIUM ACETATE 500 (CALCIUM ACETATE) ; 30-JUN-2016 / Unknown

#10) PROLIA (DENOSUMAB) ; 07-JUN-2016 / Unknown

#11) LACTULOSE AL (LACTULOSE) Syrup ; 10-NOV-2016 / Unknown

#12) FENISTIL (DIMETINDENE MALEATE) ; 17-OCT-2016 / Unknown

#13) TEVACIDOL (ALFACALCIDOL) ; 30-JUN-2016 / Unknown

#14) GLUCAGEN HYPOKIT (GLUCAGON HYDROCHLORIDE) ; 18-JUL-2016 / Unknown

#15) RENVELA (SEVELAMER CARBONATE) ; 25-AUG-2016 / Unknown

#16) RENAGEL (SEVELAMER HYDROCHLORIDE) ; 25-AUG-2016 / Unknown

#17) NEPHROTRANS (SODIUM BICARBONATE) ; 11-NOV-2016 / Unknown

#18) CEFUHEXAL 250 (CEFUROXIME AXETIL) ; 06-DEC-2016 / Unknown

#19) FERRLECIT (FERRIC SODIUM GLUCONATE COMPLEX) Injection, 62.5 mg; 19-NOV-2016 / Unknown

#20) AMBROXOL CT (AMBROXOL HYDROCHLORIDE) Injection ; 03-NOV-2015 / Unknown

Mfr. Control Number: 2016583774

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#21) PARICALCITOL RATIOPHARM (PARICALCITOL) 5 ug/ml; 28-JUL-2016 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2014 to 2015	Relevant Med History	Bladder cancer (Bladder cancer);
Unknown to Ongoing	Relevant Med History	Hemodialysis (Haemodialysis);
2013 to Ongoing	Relevant Med History	COPD (Chronic obstructive pulmonary disease);
2010 to Ongoing	Relevant Med History	Chronic right ventricular failure (Chronic right ventricular failure);
2013 to Unknown	Relevant Med History	Chronic bronchitis (Bronchitis chronic);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	08	NOV	1939	77 Years	Male	82.00 kg	20	FEB	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
myocardial infarction [Myocardial infarction]
Cardiac decompensation [Cardiac failure]
Sepsis [Sepsis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 06-MAR-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IU, 3x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 23-SEP-2014 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CONCOR COR (BISOPROLOL FUMARATE) ; Unknown / 05-MAR-2017
#2) TULIP (ATORVASTATIN CALCIUM) ; Unknown / 05-MAR-2017
#3) EDEMID (FUROSEMIDE) ; Unknown / 03-MAR-2017
#4) SEVELAMER (SEVELAMER) ; Unknown / 27-FEB-2017
#5) ZEMPLAR (PARICALCITOL) ; Unknown / 25-FEB-2017
#6) NOVORAPID (INSULIN ASPART) ; Unknown / 05-MAR-2017

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2012 to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease)
2010 to Ongoing	Relevant Med History	Amputation of both legs due to diabetes vascular complications.

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017098040

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-MAR-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a report from a non-interventional study, Protocol EPOE-09-11, regarding subject CR0050002. This 77-year-old Caucasian male subject, described as not Hispanic or Latino, started to receive treatment with epoetin zeta (RETACRIT) 6000 IU subcutaneously 3 times weekly since 23Sep2014 for renal anemia. The last dose of epoetin zeta prior to the event was on 28Feb2017. The batch number was 6T043W6, 6Q019Q6. The mean dose 1 on 24Feb2017 was 219.5 IU/kg/w when hemoglobin was 87 g/l; mean dose 2 on 24Jan2017 was 195.1 when hemoglobin was 83 g/l. It was reported that there were dose changes within 3 months prior to event, since 24Feb2017 with a new dose at 219.5 IU/kg/w. The hemoglobin prior to dose change was 83 g/l and after dose change was 87 g/l. The subject was exposed to other erythropoeitin stimulating agents (ESA), including NEORECORMON from Mar2012 to Sep2014 at 25 IU/kg/week with haemoglobin at 111 g/l. The subject did not experience any thromboembolic event during treatment with any other ESA. The subject's medical history included coronary heart disease since 2012, peripheral arterial disease since 2010 with amputations of both legs due to diabetes vascular complications, arterial hypertension since 1995, and diabetes mellitus since 1996, myocardial infarction since 2012 status post CABG x 3 in 2012, all ongoing, and hyperlipidemia. The subject was on hemodialysis. The subject's risk factors included obesity (BMI 28.67) and smoking (the patient was an ex-smoker). The subject did not have any of the following risk factors: factor V Leiden, protein C or S deficiency, antithrombin III deficiency, prothrombin G20210A mutation, homocysteinemia, recent surgery, trauma, significant and short term weight changes due to fluid retention/excretion, vascular anomalies, aneurysm, immobilization, positive family history. The subject did not have atrial fibrillation, cancer, chronic gastrointestinal disease, or diarrhea. His concomitant medications included bisoprolol fumarate (CONCOR COR) 25 mg once daily for coronary heart disease until 05Mar2017, atorvastatin calcium (TULIP) 40 mg once daily for coronary heart disease and hyperlipoproteinemia until 05Mar2017, furosemide (EDEMID) 125 mg once daily for heart disease until 03Mar2017; sevelamer 800 mg orally twice daily until 27Feb2017 and paricalcitol (ZEMPLAR) 4 mg orally once daily until 25Feb2017, both for hyperphosphatemia; all taken by mouth, insulin aspart (NOVORAPID) 19 units 3 times daily and insulin glargine (LANTUS) 24 units once daily, both subcutaneously for diabetes until 05Mar2017; glyceryl trinitrate (NITROLINGUAL) spray sublingually as needed for heart disease, all products ongoing. The subject was hospitalized on 20Feb2017 due to cardiac decompensation. On 26Feb2017 and 27Feb2017, the subject's condition was complicated with chills and increased body temperature. The subject developed sepsis, reported as 2 hemocultures of Seratia marcescens which was isolated and the therapy with cefuroxime was initially started which was changed to ciprofloxacine. On 01Mar2017, the subject's condition deteriorated, and lab tests indicated he had a myocardial infarction. Test data included cardioselective enzimes (HS troponin I) on 01Mar2017 which was reported as 21322.3 ng/l (normal range <34.2): indicating myocardial infarction. Inflammatory parameters, cardioselective enzymes and transaminase were increased and an electrocardiogram (ECG) showed posterior myocardial infarction. During the hospitalization, he had MSCT of thorax and abdomen which showed suspected neoplasm changes in both kidneys. Neoplasm of prostate was also suspected since PSA was 85.12 ug/l. The subject received standard treatment for the myocardial infarction. The standard treatment included dalteparin (FRAGMIN) 2 x 7500 IU subcutaneously, atorvastatin 40 mg orally plus previous concomitant therapy. Alteparin dosage was increased to the full therapeutic dosage. Despite all of the treatment, deterioration in general condition and of consciousness occurred and the subject died on 06Mar2017 at 5:54. The event myocardial infarction, was considered serious for hospitalization, life-threatening, and fatal with an onset date of 01Mar2017. The events cardiac decompensation with onset date of 20Feb2017 and sepsis with onset date of 27Feb2017 were considered serious for hospitalization, important medical event, life-threatening and fatal. There was no action taken with the study drug in response to the event. Autopsy was not performed. According to the hospital discharge letter, the cause of death was cardiac decompensation, sepsis (Serratia marcenscens), and myocardial infarction. The investigator reported there was not a reasonable possibility that the events, myocardial infarction, cardiac decompensation and sepsis, were related to the study drug or any concomitant drugs. Causality with regard to clinical trial procedure was not reported.

Follow-up (09Mar2017): Updates outcome to fatal, medical history, study drug details, treatment details, concomitant medication details.

Follow-up (12Mar2017 and 15Mar2017): Adds 2 events (cardiac decompensation and sepsis; both with hospitalization and life-threatening serious criteria), and updates study drug details, no past drug events with other ESAs, concomitant medications, event details, treatment, no autopsy was available, and test data.

Follow-up (22Mar2017): Updates mean dose 2 date and value, cause of death details, onset date, seriousness criteria and causality to concomitant medications for events sepsis and cardiac decompensation.

Case Comment: The Company considered there was a reasonable possibility that the reported myocardial infarction was related to epoetin zeta based on the known safety profile of the product. In addition, underlying coronary heart disease, arterial hypertension, diabetes mellitus and 'cardial' infarction in the past were significant risk factors in causing the event. The events of cardiac decompensation and sepsis were assessed as unrelated to epoetin zeta. Sepsis was due to intercurrent Seratia marcescens infection and cardiac decompensation was due to the patient's underlying cardiac conditions. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-MAR-2017	Alanine aminotransferase	5760 IU/l	48 12
2	01-MAR-2017	Aspartate aminotransferase	6950 IU/l	38 11

Mfr. Control Number: 2017098040

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
3	24-FEB-2017	Band neutrophil count	%	2 0
4	01-MAR-2017	Band neutrophil count	23.0 %	2 0
5	01-MAR-2017	Basophil count	0.0 %	1 0
6	01-MAR-2017	Blood alkaline phosphatase	134 IU/l	142 60
7	01-MAR-2017	Blood bilirubin	22 umol/l	20 3
8	24-FEB-2017	Blood calcium	2.47 mmol/l	2.53 2.14
9	15-DEC-2016	Blood cholesterol	4.2 mmol/l	
10	01-MAR-2017	Blood creatine phosphokinase	5957 IU/l	177
11	02-MAR-2017	Blood culture	Serratia marcescens	
12	20-FEB-2017	Blood glucose	6.4	
13	01-MAR-2017	Blood lactate dehydrogenase	5313 IU/l	241
14	24-FEB-2017	Blood phosphorus	1.29 mmol/l	1.42 0.79
15	24-FEB-2017	Blood potassium	4.4 mmol/l	5.1 3.9
16	21-FEB-2017	Blood pressure measurement	150/70 mmHg	
17	15-DEC-2016	Blood triglycerides	2.2 mmol/l	
18		Body mass index	28.67	
19	01-MAR-2017	C-reactive protein	226.3 mg/l	5.0 0.0
20	01-MAR-2017	Eosinophil count	0.0 %	7 0
21	01-MAR-2017	Gamma-glutamyltransferase	83 IU/l	55 11
22	24-FEB-2017	Haematocrit	0.288	0.530 0.415
23	01-MAR-2017	Haematocrit	0.291	0.530 0.415
24		Haemoglobin	111 g/l	175 138
25	24-JAN-2017	Haemoglobin	83 g/l	175 138
26	24-FEB-2017	Haemoglobin	87 g/l	175 138
27	01-MAR-2017	Haemoglobin	88 g/l	175 138
28	01-MAR-2017	Lymphocyte count	3.0 %	46 20

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
29	24-FEB-2017	Mean cell haemoglobin	25.7 pg	33.9 27.4
30	01-MAR-2017	Mean cell haemoglobin	25.2 pg	33.9 27.4
31	24-FEB-2017	Mean cell haemoglobin concentration	303 g/l	345 320
32	01-MAR-2017	Mean cell haemoglobin concentration	303 g/l	345 320
33	24-FEB-2017	Mean cell volume	84.8	97.2 83.0
34	01-MAR-2017	Mean cell volume	82.9	97.2 83.0
35	24-FEB-2017	Mean platelet volume	6.0	10.4 6.8
36	01-MAR-2017	Mean platelet volume	10.9	10.4 6.8
37	01-MAR-2017	Monocyte count	3.0 %	12 2
38	01-MAR-2017	Neutrophil count	71.0 %	72 44
39	24-FEB-2017	Platelet count	208 x10 9/l	424 158
40	01-MAR-2017	Platelet count	154 x10 9/l	424 158
41	01-MAR-2017	Procalcitonin	24.16	
42	FEB-2017	Prostatic specific antigen	85.12	
43	24-FEB-2017	Red blood cell count	3.40 x10 12/l	5.72 4.34
44	01-MAR-2017	Red blood cell count	3.50 x10 12/l	5.72 4.34
45	24-FEB-2017	Red cell distribution width increased	18.5 %	15.0 9.0
46	01-MAR-2017	Red cell distribution width increased	18.5 %	15.0 9.0
47	01-MAR-2017	Troponin I	21322.30	34.2
48	24-FEB-2017	White blood cell count	9.4 x10 9/l	9.7 3.4
49	01-MAR-2017	White blood cell count	25.1 x10 9/l	9.7 3.4

13. Relevant Tests

HS troponin I (01Mar2017): 21322.3 ng/l (normal range <34.2): indicates myocardial infarction
MSCT thorax and abdomen (Feb2017): suspect neoplasm changes on both kidneys
PSA (Feb2017): 85.12 ug/l: suspected neoplasm of prostate

Mfr. Control Number: 2017098040

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	UNK; Unknown	Renal anemia (Nephrogenic anaemia)	Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LANTUS (INSULIN GLARGINE) ; Unknown / 05-MAR-2017

#8) NITROLINGUAL (GLYCERYL TRINITRATE) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2010 to Ongoing	Relevant Med History Amputation of both legs due to diabetes vascular complications.	Peripheral arterial disease (Peripheral arterial occlusive disease);
1995 to Ongoing	Relevant Med History 21Feb2017: 150/70 mmHg.	Hypertension arterial (Hypertension);
1996 to Ongoing	Relevant Med History 20Feb2017: 6.4 mmol/l. Tpye 2	Diabetes mellitus (Diabetes mellitus);
JAN-2012 to Ongoing	Relevant Med History 1st myocardial infarction in 2012. St. post NSTEMI	Myocardial infarction (Myocardial infarction);
2012 to Unknown	Relevant Med History	CABG (Coronary artery bypass);
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
MAR-2012 to SEP-2014	Past Drug Event 25 IU/kg/week haemoglobin 111 g/l	Neorecormon (NEORECORMON);
Unknown	Relevant Med History BMI 28.67	Obesity (Obesity);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown to Ongoing	Relevant Med History 15Dec2016: Cholesterol 4.2 mmol/l, Triglycerides 2.2 mmol/l.	Hyperlipidemia (Hyperlipidaemia);
APR-2016 to Unknown	Relevant Med History St. post NSTEMI	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Chronic renal failure (Chronic kidney disease);
Unknown	Relevant Med History	Anaemia (Anaemia);
Unknown	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism);
23-FEB-2012 to Unknown	Relevant Med History	CABG (Coronary artery bypass);
Unknown	Relevant Med History	Atherosclerosis (Arteriosclerosis);
Unknown	Relevant Med History	Hiatus hernia (Hiatus hernia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Gastritis chronic (Chronic gastritis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	20	MAR	1944	72 Years	Female	90.00 kg	24	NOV	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-Interventional study, protocol EPOE-09-11, regarding subject GR051090.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 24-NOV-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 1 DF, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 08-APR-2016 / 24-NOV-2016

19. THERAPY DURATION
#1) 231 days

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☒ NO ☐ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) LANTUS (INSULIN GLARGINE) ; Unknown / 24-NOV-2016
#2) DIAMICRON (GLICLAZIDE) ; Unknown / 24-NOV-2016
#3) DILATREND (CARVEDILOL) ; Unknown / 24-NOV-2016

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease)
Unknown	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017244407

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
02-MAR-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 72-year-old Caucasian female subject started to receive epoetin zeta (RETACRIT) 55.9 IU/kg once weekly subcutaneously on 08Apr2016 for the study indication of renal anemia. The subject's medical history included coronary heart disease, hypertension and diabetes mellitus. Her concomitant medications included insulin glargine (LANTUS) subcutaneously and gliclazide (DIAMICRON) by mouth, both for diabetes mellitus, and carvedilol (DILATREND) by mouth for coronary heart disease. On 24Nov2016, the subject died at the hospital due to a myocardial infarction. No test or treatment details were provided. The action taken with epoetin zeta was unknown. The investigator reported there was no reasonable possibility that the event, myocardial infarction, was related to the study drug or any concomitant medication.

Follow-up (02Mar2018). New information reported in this follow-up from a non-Interventional study, protocol EPOE-09-11, regarding subject GR051090 included: The investigator reported that the stop date (24Nov2016) was the actual stopping of the product. Concomitant medication included insulin glargine (LANTUS) 16 1x1, gliclazide (DIAMICRON) 60, 1x1 and carvedilol (DILATREND) 12.5 1x2 with stop date 24Nov2016.

Follow-up (02Mar2018). New information reported in this follow-up from a non-Interventional study, protocol EPOE-09-11, regarding subject GR051090 included Data Capture Aid for Retacrit and thromboembolic events.
Concomitant medication LANTUS, DIAMICRON and DILATREND stop date was 24Nov2016
The subject had never been exposed to any other erythropoietin-stimulating agents. Other risk factors included: bypass in 2011. Relevant concurrent and past diseases of the subject: hyperlipidemia, ischemic heart disease, transient ischemic attack. The subject was pre-dialysis.
No lab data were available. The subject had been admitted to the hospital because of the event. The event was life-threatening.

Follow-up attempts completed. No more information are expected.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, myocardial infarction, was related to epoetin zeta or any concomitant medication. The event was most likely due to the subject's underlying medical conditions. Underlying diseases of coronary heart disease, hypertension and diabetes mellitus along with advanced age were significant risk factors in causing the reported event. The follow up information received does not alter the previous company clinical evaluation.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
2011 to Unknown	Relevant Med History	Bypass surgery (Vascular graft);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
PRIVACY	GREECE	30	APR	1934	82 Years	Male	70.00 kg	07	JUL	2016	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

heart attack [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II).

This is a report from a Pfizer-sponsored non-interventional study, protocol EPOE-09-11, regarding subject GR051085.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 07-JUL-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 5000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-FEB-2016 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) LASIX /00032601/ (FUROSEMIDE) ; Ongoing
#2) LANTUS (INSULIN GLARGINE) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus)
FEB-2016 to Unknown	Relevant Med History	Heart failure (Cardiac failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017253323

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JUL-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 82-year-old Caucasian male subject started epoetin zeta 5000 IU weekly subcutaneously on 15Feb2016 for the study indication renal anemia. His medical history was significant for type 2 diabetes mellitus and cardiac failure since Feb2016. The subject did not experience any thromboembolic event during treatment and had no exposure to any other erythropoietin stimulating agent (ESA). He had no risk factors for thromboembolic events. Concomitantly, he was on furosemide (LASIX) 40 mg orally once daily for heart failure and insulin glargine (LANTUS) at 10 IU subcutaneously once daily for type 2 diabetes mellitus; both products ongoing at the onset of the event. On 07Jul2016, the subject experienced a heart attack and died on the same day. An autopsy was not performed. Diagnostic test results performed to establish the diagnosis/adverse reaction were not available. The investigator reported that there was no reasonable possibility that the event, heart attack, was related to the study drug or to any concomitant medication.

Follow-up (12Jul2017): Updates event data, tests, subject data, and concomitant medications.

Follow-up attempts are completed. No further information is expected.

Follow-up (17Jul2017): Updates concomitant medication details, history.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, heart attack was related to epoetin zeta therapy. The patient's elderly age and pre-existing multimorbidity, including type 2 diabetes mellitus and cardiac failure, were significant risk factors for development of the event.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	22	AUG	1936	79 Years	Female	91.00 kg	14	OCT	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Vascular stroke [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from non-interventional study, Protocol C1111006, regarding subject GR0340010.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 14-OCT-2015
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 8000 IU, 2x/week (87.9/kg/week)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) OCT-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) LANTUS (INSULIN GLARGINE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension)
Unknown	Relevant Med History	Diabetes (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
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Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017358127

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-OCT-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2017358127

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 79-year-old Caucasian female subject started to receive epoetin zeta (RETACRIT) 8000 IU subcutaneously twice a week (87.9/kg/week) in Oct2014 for study indication of renal anemia. The subject's medical history was significant for hypertension, diabetes, hyperlipidemia, and heart failure. Concomitantly, the subject was taking insulin glargine (LANTUS) subcutaneously once daily for diabetes. The subject was not exposed, at any time, to any other erythropoietin stimulating agent (ESA). Her hemoglobin on 07Jul2015 was 11 g/dl. The subject was under peritoneal dialysis. The subject died of vascular stroke on 14Oct2015, which was also reported to be life-threatening. The site staff was informed about this event on 24Feb2017. An autopsy was not performed. The investigator reported that there was not a reasonable possibility that the event, vascular stroke, was related to the study drug or to a concomitant drug.

Follow-up (05Oct2017): Updates test data, medical history, concomitant medication data, seriousness criteria, and general data regarding the subject.

Follow-up attempts completed. No further information is expected.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event vascular stroke was related to the study drug epoetin zeta. Advanced age, pre-existing conditions of diabetes mellitus, hypertension, hyperlipidemia and heart failure were considered as significant risk factors to the development of vascular stroke.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-JUL-2015	Haemoglobin	11 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Heart failure (Cardiac failure);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	20	NOV	1941	74 Years	Male	67.00 kg	05	APR	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart attack [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a contactable physician from a non-interventional study report, Protocol C1111006, regarding subject GR0340009.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 05-APR-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, 2x/week (149.2/Kg/week)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 16-JAN-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension)
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017358130

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-OCT-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 74-year-old Caucasian male subject started to receive epoetin zeta (RETACRIT) 10000 IU subcutaneously two times a week (149.2/Kg/week) on 16Jan2014 for the study indication of nephrogenic anemia. The subject's medical history included hypertension and hyperlipidemia. The subject underwent peritoneal dialysis. On 01Mar2016, the subject's hemoglobin was 11 g/dl. He was not exposed to any other erythropoietin stimulating agent (ESA) at any time. The subject's concomitant medications were not reported. The subject died on 05Apr2016 due to heart attack, also considered serious for life threatening. An autopsy was not performed. The investigator considered that there was not a reasonable possibility that the event, heart attack, was related to the study drug or any concomitant medications.

Follow-up (05Oct2017): Updates seriousness criteria, study drug details, subject details, medical history, tests.

Follow-up attempts are completed. No further information is expected

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, heart attack was related to epoetin zeta therapy. The subject's elderly age and pre-existing hypertension and hyperlipidemia were risk factors for development of the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-MAR-2016	Haemoglobin	11 g/dl	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	22	DEC	1941	75 Years	Female	50.00 kg	22	SEP	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

suspected of heart attack [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11, regarding subject GE-094-0032.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 22-SEP-2017
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK, 3x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 14-SEP-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
MAY-2011 to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease)
DEC-2011 to Unknown	Relevant Med History	
	Stage IV left foot	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017435221

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-OCT-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old Caucasian female subject started to receive epoetin zeta (RETACRIT), dose unspecified, 3 times weekly on 14Sep2015 for the study indication of nephrogenic anemia. On 09Aug2017, the subejct started to receive epoetin zeta 1000 subcutaneously twice weekly and 5000 once weekly; on 22Sep2017, she received the last dose. The subject's medical history was significant for coronary heart disease, also reported as ischemic heart disease, since May2011, peripheral artery disease (PAD) stage IV left since Dec2011, hypertension since May2011, atrial fibrillation, all ongoing, and cancer (plasmocytoma) since Jun2016 and mamma carcinoma left first diagnosis in Feb2017. The subject had not received any other erythropoietin stimulating agents. Also, in Jul2017 a percutaneous transluminal angioplasty (PTA) was performed without complications in hospital for an unspecified indication. No concomitant medications were reported. On 10Jul2017, the subject's hemoglobin (Hgb) was 10.9g/dL (normal range 11.3-15.5), hematocrit (Hct) 33.3% (25.4 to 49.1), C-reactive protein (CRP) 15 mg/L (normal < 5), and red blood cell (RBC) count was 3.83 x 10 6/mm3 (3.82-5.3). On 07Aug2017: CRP 1.6 mg/L, Hct 28.9%, Hgb 9.3 g/dL, and RBC 3.22. On 11Sep2017, the subject's Hgb was 10.5 g/dL, Hct 33% (35.4-49.1), RBC 3.6, and CRP 1.4 mg/L. On 22Sep2017, the subject was "suspected of heart attack" and died. The cause of death was reported as "suspected of heart attack of coronary heart disease". No tests or treatment details were provided. No autopsy was performed. The investigator reported that there was not a reasonable possibility that the event, suspected of heart attack, was related to the study drug or to any concomitant medication.

Follow-up (17Oct2017): Updates study drug data, provides tests, updates medical history.

Follow up (19Oct2017): Updated medical history.

Case Comment: In agreement with the investigator, the company considered there was not a reasonable possibility that the event suspected heart attack was related to epoetin zeta The event was probably due to underlying cardiovascular conditions. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	10-JUL-2017	C-reactive protein	15 mg/l	5
2	07-AUG-2017	C-reactive protein	1.6 mg/l	5
3	11-SEP-2017	C-reactive protein	1.4 mg/l	5
4	10-JUL-2017	Haematocrit	33.3 %	49.1 35.4
5	07-AUG-2017	Haematocrit	28.9 %	49.1 35.4
6	11-SEP-2017	Haematocrit	33 %	49.1 35.4
7	10-JUL-2017	Haemoglobin	10.9 g/dl	15.5 11.3
8	07-AUG-2017	Haemoglobin	9.3 g/dl	15.5 11.3
9	11-SEP-2017	Haemoglobin	10.5 g/dl	15.5 11.3
10	10-JUL-2017	Red blood cell count	3.83 x10 6/mm3	5.3 3.82
11	07-AUG-2017	Red blood cell count	3.22 x10 6/mm3	5.3 3.82
12	11-SEP-2017	Red blood cell count	3.6 x10 6/mm3	5.3 3.82

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution	5000, weekly;	nephrogenic anemia	09-AUG-2017 /

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
for injection; Regimen #2	Subcutaneous	(Nephrogenic anaemia)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	10000, 2x/week; Subcutaneous	nephrogenic anemia (Nephrogenic anaemia)	09-AUG-2017 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
DEC-2011 to Unknown	Relevant Med History Stage IV left foot	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease);
APR-2011 to Ongoing	Relevant Med History stop date: unknown	Hypertension (Hypertension);
JUL-2017 to JUL-2017	Relevant Med History PTA without complications	Surgery (Surgery);
MAY-2011 to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
JUN-2016 to Unknown	Relevant Med History Mamma carcinoma left (Feb2017 First diagnosis)	Cancer (Neoplasm malignant);
FEB-2017 to Unknown	Relevant Med History Mamma carcinoma left	Breast carcinoma (Breast cancer);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	08	JUL	1930	87 Years	Male	82.00 kg	30	AUG	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer-sponsored non-interventional study, Protocol EPOE-09-11, regarding subject ES0240038.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 30-AUG-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 5000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 02-MAY-2016 / 30-AUG-2017

19. THERAPY DURATION
#1) 486 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
02-MAY-2016 to Unknown	Relevant Med History	Renal failure (Renal failure)
2002 to Ongoing	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017447054

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2017447054

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 87-year-old Caucasian male subject started treatment with epoetin zeta 5000 IU administered subcutaneously weekly from 02May2016 to 30Aug2017 for renal anemia. The subject's medical history included renal failure since 02May2016, ischaemic heart disease from 2002 and ongoing, hypertension, atrial fibrillation, cancer (not specified), chronic gastrointestinal disease, diarrhoea. No concomitant medications were reported. On 30Aug2017, the subject experienced an acute myocardial infarction and died. The status of epoetin zeta at the time of the subject's death was unknown. An autopsy was not performed. The investigator reported that the event, acute myocardial infarction, was unrelated to the study drug and to any concomitant drug.

Follow-up (23Nov2017): updated Relevant Med History.

Case Comment: In agreement with the investigator, Company considered that there was not a reasonable possibility that the event "myocardial infarction" was related to study drug. Subject's advanced age was a significant risk factor. Additional information including relevant medical history, concomitant medications and detailed clinical course around the event etc, is required to better assess the case.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	20-JUN-2017	Haemoglobin	11.5 g/dl	
2	23-AUG-2017	Haemoglobin	10.1 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History not specified	Cancer (Neoplasm malignant);
Unknown	Relevant Med History	Gastrointestinal disorder (Gastrointestinal disorder);
Unknown	Relevant Med History	Diarrhoea (Diarrhoea);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	28	FEB	1949	68 Years	Female	90.00 kg		JUN	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

brain's stroke [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer-sponsored non-interventional study, protocol EPOE-09-11, regarding subject BG006039.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: JUN-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 ug, 3 times weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 23-SEP-2015 / FEB-2017

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN MIX (INSULIN HUMAN, INSULIN HUMAN INJECTION,
#2) BISOR (BISOPROLOL FUMARATE) ; 2015 / 2017
#3) NORDIPIN (AMLODIPINE MESILATE) ; 2015 / 2017
#4) BETASERC /00141801/ (BETAHISTINE) ; FEB-2017 / APR-2017
#5) FURANTHRIL /00032601/ (FUROSEMIDE) ; 1988 / 2017
#6) KARDIKET (ISOSORBIDE DINITRATE) ; 2016 / 2017

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Cervix carcinoma (Cervix carcinoma)
1988 to Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017489626

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 68-year-old Caucasian female subject started to receive epoetin zeta (RETACRIT) at 4000 mcg 3 times weekly from 23Sep2015 for renal anemia. The batch number was not available. Study drug epoetin zeta stop date reported as Feb2017. Her medical history was significant for cancer (carcinoma of cervix), chronic gastrointestinal disease (cholecystectomy) in 1987, hyperlipidemia since 1988, ischemic heart disease since 1988, peripheral arterial disease since 1988, diabetes mellitus since 1988 and hypertension since 1988, thyroidectomy since 1988, transient ischemic attack in 2010, kidney failure in 2011,brain's stroke- first in 2010, carcinoma coli uteri with hysterectomy since 1987, nephrolithiasis - pelvilithotomy on both side, heart failure, thyroid disease-with total thyroidectomy 1988. The subject was pre-dialysis. Risk factor for thromboembolic events reported as obesity from 1988 and body mass index (BMI) reported as 32.66. The subject was not exposed any other erythropoietin stimulating agent. Concomitantly, she was on insulin human, insulin human injection, isophane (INSULIN MIX 25) with 46 E, 3x/day since 2008 for diabetes mellitus, bisoprolol fumarate (BISOR) with 5 mg once daily from 2015 to 2017 for hypertension and amlodipine mesilate (NORDIPIN) with 5 mg once daily from 2015 to 2017 for hypertension, furosemide (FURANTHRIL) with 40 mg once daily from 1988 to 2017 for hypertension, isosorbide dinitrate (KARDIKET) with 20 mg twice daily from 2016 to 2017 for hypertension and heart failure, acetylsalicylic acid (ASPIRIN PROTECT) with 100 mg once daily for with unknown start date to 2017 for heart failure and IHD (ischaemic heart disease), betahistine (BETASERC) with16 mg three times daily for brain's stroke from Feb2017 to Apr2017, and moxonidine (MOXOGAMMA) with 4 mg once daily from 2017 to 2017 for hypertension. Hemoglobin was reported as 10.5 g/dl. Three months prior the event, the dose was not changed. The subject did not have any thromboembolic event during treatment. On an unspecified date, the subject experienced a "brain's stroke", which was the cause of her death in Jun2017. The subject was hospitalized because of the event brain's stroke and the event was life-threatening. Onset date of adverse event brain's stroke reported as Jun2017. A hospital discharge letter was not available. The action taken in response to the event for epoetin zeta was post-therapy. Laboratory/ diagnostic results were not available. Diagnostic test results performed to established the diagnosis/ adverse reaction (myocardial infraction; cerebrovascular incident and pulmonary embolism) were not available. An autopsy was not performed. The investigator reported that there was not a reasonable possibility that the event brain's stroke was related to the study drug or to a concomitant drug.

Follow-up (15Nov2017 and 16Nov2017): New information reported from the same contactable physician includes: study drug data, dialysis status, medical history, no previous history of erythropoietin stimulating agent use, concomitant medications, event details, and serious criteria (life-threatening and hospitalization).

Follow-up (27Nov2017): New information reported from the same contactable physician includes: new relevant medical history, updated concomitant drugs information and new concomitant drug (moxonidine), updated epoetin zeta dose stop date and event onset date.

No follow-up attempts are possible; information about batch number cannot be obtained.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, brain's stroke, was related to the study drug epoetin zeta or concomitant drugs. The patient's underlying cardiovascular conditions including transient ischemic attack, diabetes and hypertension provided an explanation for the reported event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body mass index	32.66	
2		Haemoglobin	10.5 g/dl	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) INSULIN MIX (INSULIN HUMAN, INSULIN HUMAN INJECTION, ISOPHANE) ; 2008 / Unknown

#7) ASPIRIN PROTECT (ACETYLSALICYLIC ACID) ; Unknown / 2017

#8) MOXOGAMMA (MOXONIDINE) ; 2017 / 2017

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1988 to Unknown	Relevant Med History	Hypertension (Hypertension);
1987 to Unknown	Relevant Med History	Carcinoma uterine cervix (Cervix carcinoma);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Hysterectomy	
Unknown	Relevant Med History	Hysterectomy (Hysterectomy);
1987 to Unknown	Relevant Med History Cholecystectomy	Gastrointestinal disorder (Gastrointestinal disorder);
1988 to Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
1988 to Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
1988 to Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
1988 to Unknown	Relevant Med History	Thyroidectomy (Thyroidectomy);
2010 to Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
2011 to Unknown	Relevant Med History	Kidney failure (Renal failure);
1988 to Unknown	Relevant Med History BMI 32,66	Obesity (Obesity);
2010 to Unknown	Relevant Med History	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History pelvilithotomy on both side	Nephrolithiasis (Nephrolithiasis);
Unknown	Relevant Med History	Heart failure (Cardiac failure);
Unknown	Relevant Med History 1988 thyroidectomy total	Thyroid disorder (Thyroid disorder);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	25	MAY	1944	73 Years	Male	85.00 kg	26	OCT	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study protocol EPOE-09-11 for subject ID BG025011.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 27-OCT-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 08-MAY-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SINTROM (ACENOCOUMAROL) Tablet ; Unknown / 2017
#2) PHYSIOTENS (MOXONIDINE) Tablet ; 1998 / 2017
#3) PRESTARIUM (PERINDOPRIL) Tablet ; 1998 / 2017
#4) FURANTHRIL (FUROSEMIDE) Tablet ; 1998 / 2017

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2011 to Unknown	Relevant Med History	Chronic kidney disease (Chronic kidney disease)
2002 to Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017495875

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
29-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old male Caucasian non-Hispanic or Latino subject started to receive epoetin zeta (RETACRIT) at 3000 IU once weekly on 08May2015 for renal anemia. No dose changes were made within three months prior to the event. The subject was not exposed to any other erythropoietin- stimulating agent (ESA). The subject did not experience any thromboembolic event during treatment with any other ESA. The subject's medical history was significant for chronic kidney disease since 2011, diabetes mellitus since 2002, hypertension since 1998, vascular anolamies (diabetic microangiopathy), ischemic heart disease, peripheral arterial disease, and atrial fibrillation. The subject does not receive dialysis (pre-dialysis) Concomitant medications included acenocoumarol (SINTROM) 4 mg (0.5 tablet) daily from an unspecified date to an unspecified date in 2017 for atrial fibrillation, moxonidine (PHYSIOTENS) 0.2 mg (1 tablet) twice daily from 1998 to 2017 for hypertension, perindopril (PRESTARIUM) 5 mg (1 tablet) once daily from 1998 to 2017 for hypertension, and furosemide (FURANTHRIL) 40 mg (1 tablet) once daily from 1998 to 2017 for hypertension. Risk factors for thromboembolic events include vascular anomalies - diabetic macroangiopathy. The subject experienced myocardial infarction on 26Oct2017 and died on 27Oct2017. The subject was admitted to hospital because of the event from 26Oct2017 to 27Oct2017. The event was also considered life threatening. Laboratory/ diagnostic results reported included hemoglobin 102 g/l; hematocrit 0.29 g/l; red blood cells 3.16 g/l; ECG readings- asystolia --> ventricular fibrillation--> Abs. arrhythmia in atrial fibrillation, HR82; echocardiography - dilated atria, dilated right ventricle, suppressed systolic function at rest, hypokinesia of the upper left ventricular segments; troponin I and T - troponin T-HS 0.1--> 1.8 ng/ml (26Oct2017); creatinine kinase (including CKMB isoenzyme)- CK- 144.03--> 1282.66 U/l (26Oct2017), CK- MB- 39.83--> 113.65 U/l (26Oct2017); angiography - coronary atherosclerosis, acute anterior myocardial infarction, ventricular fibrillation, cardiogenic shock, hemoglobin on 26Oct2017: 102 g/l (range 140- 180) and troponin T-HS on unknown date: 0.105; 0.525 ng/ml (range 0.01- 0.03). Action taken with suspect drug was unknown. An autopsy was not performed and the reported cause of death was myocardial infarction. The investigator considered that there was not a reasonable possibility that the event myocardial infarction was related to the study drug or to a concomitant drug.

Follow-up (21Nov2017): Updates medical history, study drug details, event details, tests

Follow-up (29Nov2017): Updates concomitant medication details, tests

The follow-up is being submitted to notify that the batch number is not available despite the Follow-up attempts made.

Follow-up attempts have been completed and no further information is expected.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event myocardial infarction leading to the subject's demise was related to the study drug epoetin zeta or to a concomitant drug. The subject's elderly age and pre-existing multimorbidity including diabetes mellitus and hypertension were significant risk factors for development of myocardial infarction. The follow up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Angiogram	coronary atherosclerosis	
2		Blood creatine phosphokinase	144.03	
3	26-OCT-2017	Blood creatine phosphokinase	1282.66	
4		Blood creatine phosphokinase MB	39.83	
5	26-OCT-2017	Blood creatine phosphokinase MB	113.65	
6		Echocardiogram	dilated atria	
7		Electrocardiogram	asystolia	
8		Haematocrit	0.29 g/l	
9		Haemoglobin	102 g/l	180 140
10	26-OCT-2017	Haemoglobin	102 g/l	180 140
11		Heart rate	82	

Mfr. Control Number: 2017495875

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
12		Red blood cell analysis	3.16 g/l	
13		Troponin T	0.1 ng/ml	
14		Troponin T	0.525 ng/ml	0.03 0.01
15		Troponin T	0.105 ng/ml	0.03 0.01
16	26-OCT-2017	Troponin T	1.8 ng/ml	

13. Relevant Tests

ECG (unknown date) - asystolia -ventricular fibrillation Abs. arrhythmia in atrial fibrillation,HR82
Echocardiography (unknown date) - dilated atria, dilated right ventricle, suppressed systolic function at rest, hypokinesia of the upper left ventricular segments
Troponin I and T (unknown date) - troponin T-HS 0.1 --> 1.8 ng/ml
Creatinine kinase (including CKMB isoenzyme)(unknown date) - CK- 144.03 --> 1282.66 U/l, CK- MB- 39.83--> 113.65 U/l
Angiography(unknown date) - coronary atherosclerosis, acute anterior myocardial infarction, ventricular fibrillation, cardiogenic shock
Troponin T-HS (unknown date) - 0,105 ng/ml (range 0.01- 0.03) - high
Troponin T-HS (unknown date) - 0,525 ng/ml (range 0.01- 0.03) - high

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1998 to Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History diabetic macroangiopathy	Vascular anomaly (Vascular malformation);
Unknown	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	27	FEB	1943	74 Years	Male	Unk	26	AUG	2017	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study source for protocol EPOE-90-11 (C1111006), subject IT120033.
A 74 Years-old, Caucasian, Male subject started to receive EPOETIN

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 30-AUG-2017
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 10000 IU, three times for week

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FUROSEMIDE (FUROSEMIDE) ; Ongoing
#2) ATORVASTATINA (ATORVASTATIN CALCIUM) ; Ongoing
#3) INSULINA /00030501/ (INSULIN) ; Ongoing
#4) CALCITRIOLO (CALCITRIOL) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)
Unknown to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018006285

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-JAN-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2018006285

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

ZETA (Epoetin Zeta, Solution for injection) at 10000 IU, three times for week via an unspecified route of administration from an unspecified date for an unspecified indication. The subject had a relevant history of ongoing diabetes mellitus, ongoing chronic kidney disease and ongoing hypertension. Concomitant medications included furosemide (FUROSEMIDE), atorvastatin calcium (ATORVASTATINA), insulin (INSULINA /00030501/) and calcitriol (CALCITRIOLO), all ongoing. On 26Aug2017 the subject experienced Acute myocardial infarction on 26Aug2017 with fatal outcome. The action taken with product Epoetin Zeta was not applicable. The subject died from Acute myocardial infarction on 30Aug2017. An autopsy was not performed.
The investigator considered that the relationship of the event to treatment with Epoetin Zeta and concomitant medications was unrelated.

Case Comment: Based on the available information the event: Acute myocardial infarction (fatal) is most likely related to an intercurrent or underlying condition which is not related to the subject drug.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
PRIVACY	GREECE	08	JAN	1970	47 Years	Male	79.00 kg	10	FEB	2017	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

heart infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional study report for Protocol EPOE-09-11, POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 10-FEB-2017
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 10000 IU, 3/w	#1) Unknown

☐ YES ☐ NO ☒ NA

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-OCT-2016 / Unknown	#1) Unknown

☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2013 to 10-FEB-2017	Relevant Med History	Hypertension (Hypertension)
2013 to 10-FEB-2017	Relevant Med History	Nephropathy (Nephropathy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018036059

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-JAN-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II), regarding subject GR059006. A 47 year-old Caucasian male subject started Epoetin Zeta, 10000 IU, 3/w (as reported) via an unspecified route of administration on 12Oct2016 for renal anemia. The subject medical history included hypertension and nephropathy. Concomitant drugs was unknown. On 10Feb2017 the subject experienced heart infarction. The action taken with epoetin zeta was Not Applicable. The event was fatal. The subject died due to the heart infarction on 10Feb2017. An autopsy was not performed. The investigator considered that there was not a reasonable possibility that the event heart infarction was related to study drug or any concomitant medication.

Case Comment: In Agreement with the investigator's assessment, the Company considered there was not a reasonable possibility that the reported heart infarction with fatal outcome was related to the Epoetin Zeta. Patient's underlying hypertension may be regarded as the most likely explanation for the event.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	01	JAN	1937	80 Years	Female	68.50 kg		AUG	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional study report for Protocol EPOE-09-11 (C1111006).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 20-AUG-2017
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 5000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-SEP-2016 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SALUREX (FUROSEMIDE) ; 21-FEB-2017 / AUG-2017
#2) LOPRESOR [METOPROLOL TARTRATE] (METOPROLOL TARTRATE)
#3) FUROSEMIDE (FUROSEMIDE) ; 21-FEB-2017 / AUG-2017

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
23-MAY-2016 to AUG-2017	Relevant Med History	Hypertension (Hypertension)
21-SEP-2016 to AUG-2017	Relevant Med History	Heart failure (Cardiac failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018212348

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-JAN-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2018212348

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 80 year-old female subject received epoetin zeta (RETACRIT), subcutaneous from 21Sep2016 to Aug2017 at 10000 IU, 2x/week for renal anemia. The subject medical history included hypertension from 23May2016 to Aug2017, heart failure from 21Sep2016 to Aug2017. Concomitant medication included furosemide from 21Feb2017 to Aug2017 fro hypertension and heart failure. It was reported that the subject could not be reached regarding the schedule visit of the study. The study investigator manage to communicate with the subjects relatives on 23May2018 and was informed about the subjects death in Aug2017 due to myocardial infarction and the subject had been discontinued from the study. An autopsy was not performed. The investigator reported that there was not a reasonable possibility that the event myocardial infarction was related to the study drug.

Follow-up (06Jun2018). This is a follow up report from a Non-Interventional study source for Protocol EPOE-09-11 (C1111006).
The subject did not undergo any type of dialysis. On 15Jun2017 haemoglobin was 10.6 g/dl and on 10Aug2017 haemoglobin was 9.9. The dose of epoetin zeta (RETACRIT) was changed on 10Aug2017 to 10000 IU weekly. The last dose of epoetin zeta prior to the event was on 10Aug2017. Concomitant medications included furosemide (SALUREX) on 21Feb2017 at "125 no units, 1/4 of 500 x 1" and metoprolol (LOPRESOR) on 15JUn2017 at "1/4 x 3".

Follow-up (16Oct2019): This is a follow-up Non-Interventional study report for Protocol EPOE-09-11 (C1111006).
The subject experienced myocardial infarction on 20Aug2017 and died on the same day due to it.

Follow-up (08Jan2020): This is a follow-up Non-Interventional study report for Protocol EPOE-09-11 (C1111006).
Treatment dates and dosage of epoetin zeta (RETACRIT) were updated to 5000IU, 1x/week from 21Sep2016 and at 10000IU, 1x/week from 15Jun2017.

Follow-up (20Jan2020): This is a follow-up Non-Interventional study report for Protocol EPOE-09-11 (C1111006). The investigator mentioned:
Relevant medical history included hypertension from 23May2016 to Aug2017 and heart failure from 21Sep2016 to Aug2017.
Concomitant medication included furosemide from 21Feb2017 to Aug2017 fro hypertension and heart failure. The patient experienced myocardial infarction in Aug2017.

Follow-up activities completed. No further information expected.

Follow-up activities completed. No further information expected.

Case Comment: Based on the available information the event: myocardial infarction (fatal) is most likely related to an intercurrent or underlying condition which is not related to the subject drug. The follow up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	15-JUN-2017	Haemoglobin	10.6 g/dl	
2	10-AUG-2017	Haemoglobin	9.9 g/dl	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	10000 IU, weekly; Unknown	renal anemia (Nephrogenic anaemia)	15-JUN-2017 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) LOPRESOR [METOPROLOL TARTRATE] (METOPROLOL TARTRATE) ; 15-JUN-2017 / Unknown

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		MAY	1947	70 Years	Female	58.20 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

intracerebral bleeding [Cerebral haemorrhage]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11. This subject of unspecified age started to receive epoetin zeta, dose, start date and indication unspecified.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 18-APR-2018
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
#2) RIVAROXABAN (RIVAROXABAN)
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, 1x/week	#1) Subcutaneous
#2) UNK	#2) Oral

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)
#2) atrial fibrillation (Atrial fibrillation)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown	#1) Unknown
#2) 15-JAN-2018 / Unknown	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
NOV-2012 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation) anticoagulation therapy with rivaroxaban
Unknown	Relevant Med History	Kidney transplant (Renal transplant)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018308638

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-JUN-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

No medical history or concomitant medications were provided. On an unspecified date, the subject developed intracerebral bleeding. No test or treatment details were reported. The subject died on an unspecified date. The cause of death was reported as intracerebral bleeding and oral anticoagulation therapy (unspecified). It was not known if an autopsy was performed. The action taken with epoetin zeta was reported as not applicable. The physician reported the event was unrelated to epoetin zeta.

Follow-up (13Aug2018): This is a follow-up report combining information from duplicate reports 2018308638 and case 2018309947. The current and all subsequent follow-up information will be reported under manufacturer report number 2018308638. The new information reported from a non interventional study report includes:
A 70 years old female subject started to receive epoetin zeta (Retacrit), subcutaneous from unspecified date to unspecified date at 2000 IU weekly for renal anemia, rivaroxaban (reported as concomitant drug) orally from 15Jan2018 to an unspecified date at unknown dose for atrial fibrillation. Medical history included atrial fibrillation from Nov2012 and ongoing anticoagulation therapy with rivaroxaban. The subject's concomitant medications were not reported. The subject had not been present since Feb2018, subject was not reachable at home, the son of the patient gave the information, that the subject died in a hospital in another town on 18Apr2018 due to an assumed cerebral bleeding. Reporter called this hospital for further information, but because of data protection no information was available. The action taken in response to the event for epoetin zeta was unknown, for rivaroxaban was unknown. The subject died on 18Apr2018. An autopsy was not performed. The event was assessed as unrelated to Retacrit and related to concomitant drug rivaroxaban.

Follow-up (27Aug2018): New information received from the investigator includes: dosage regimens for RETACRIT 2000 IU once/week from 16Oct2017 to Apr2018; 1000 IU once/week from 17Jul2017 to 15Oct2017; 1000 IU once/week from 23May2016 to 16Jul2017;
Medical history included intermittent atrial fibrillation from Nov2012 and ongoing, renal transplant, homocystinaemia known since many years, the subject underwent surgery due to spinal stenosis from 24Jan2018 to 31Jan2018, the subject had vascular anomaly and transient ischemic attack which was further specified as appoplex putamen ileft side in 1998, hyperlipidaemia from 2007 and ongoing, peripheral arterial occlusive disease from Apr2015 and ongoing, hypertension since 1980 and ongoing, chronic heart failure from 2008 and ongoing, haemodialysis from Apr2008 to Nov2012; all other diseases, risk factors: None. Family history was unknown. The subject previously took biopoin. The subject did not experience a thromboembolic event while other erythropoetin therapy. The subject underwent lab tests and procedures which included haemoglobin: 11.3 g/dl on 03Jan2018 while Retacrit therapy 2000 IU/week , haemoglobin: 12.1 g/dl on unknown date while Biopoin therapy; the Dosis of Retacrit was not changed 3 months prior the event occurred; no other lab tests available.

Follow-up (19Jun2019): New information includes: the subject's information updated.

Case Comment: Based on the information currently provided, the company concurs with the causality assessment provided by the reporter, considering the event was unrelated to epoetin zeta. The patient's underlying cardiovascular diseases and concomitant anticoagulation therapy provided likely explanation for the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	12.1 g/dl	
2	03-JAN-2018	Haemoglobin	11.3 g/dl	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	1000 IU, 1x/week; Subcutaneous	renal anemia (Nephrogenic anaemia)	23-MAY-2016 / 16-JUL-2017; 420 days
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	1000 IU, 1x/week; Subcutaneous	renal anemia (Nephrogenic anaemia)	17-JUL-2017 / 15-OCT-2017; 91 days
#1) Epoetin Zeta (EPOETIN ZETA) Solution	2000 IU, 1x/week;	renal anemia (Nephrogenic	16-OCT-2017 /

Mfr. Control Number: 2018308638

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
for injection; Regimen #4	Subcutaneous	anaemia)	APR-2018; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
22-JAN-2013 to 02-APR-2013	Past Drug Event 5000 IU / week subcutaneous	Biopoin (BIOPOIN);
Unknown	Relevant Med History known since many years	Homocystinaemia (Homocystinaemia);
24-JAN-2018 to 31-JAN-2018	Relevant Med History	Spinal stenosis NOS (Spinal stenosis);
24-JAN-2018 to 31-JAN-2018	Relevant Med History	Spinal operation (Spinal operation);
1998 to 1998	Relevant Med History	Stroke (Cerebrovascular accident);
NOV-2012 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
2007 to Ongoing	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
APR-2015 to Ongoing	Relevant Med History	Peripheral occlusive disease (Peripheral arterial occlusive disease);
1980 to Ongoing	Relevant Med History	Hypertension (Hypertension);
APR-2008 to NOV-2012	Relevant Med History	Haemodialysis (Haemodialysis);
2008 to Ongoing	Relevant Med History	Chronic heart failure (Cardiac failure chronic);
1998 to 1998	Relevant Med History apoplex putamen left side	Vascular anomaly (Vascular malformation);
1998 to 1998	Relevant Med History apoplex putamen left side	TIA (Transient ischaemic attack);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	27	JUL	1935	83 Years	Male	82.00 kg	08	NOV	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non-Interventional study source for protocol: EPOE-09-11 (C1111006), Center ID/Subject ID: BG004094.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 18-NOV-2018
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU (2x2000) weekly	#1) Unknown

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 05-FEB-2016 / MAR-2018	#1) 1006 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NOOTROPIL (PIRACETAM) Tablet ; 2016 / 08-NOV-2018
#2) VINPOCETINE (VINPOCETINE) ; 2016 / 08-NOV-2018
#3) DIGOXIN (DIGOXIN) ; 2016 / 08-NOV-2018
#4) ASPIRIN (ACETYLSALICYLIC ACID) ; 2016 / 18-NOV-2018
#5) ROCALTROL (CALCITRIOL) ; 2016 / 08-NOV-2018
#6) AMLODIPINE (AMLODIPINE) ; 2016 / 08-NOV-2018

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Chronic pyelonephritis (Pyelonephritis chronic)
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018473550

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-NOV-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 83-year-old male subject started to receive epoetin zeta (RETACRIT) via an unspecified route of administration from 05Feb2016 to Mar2018 at 4000 IU (2x2000) weekly, subcutaneous from Mar2018 to 07Nov2018 at 6000 IU (3x2000) weekly for renal anemia. Mean dose 1 and 2 reported as 3x2000 4l weekly. The dose have not be changed within 3 months prior to the event. Medical history included chronic pyelonephritis from unknown date and ongoing; hypertension on an unknown date and ongoing; kidney polycystic disease since Nov2014 and ongoing; anemia since 02Feb2016 and ongoing; and ischaemic heart disease from an unspecified date. Concomitant medication included piracetam (NOOTROPIL) 2x 1 tablet orally taken for dementia from 2016 to 08Nov2018, vinpocetine 2x5mg orally taken for dementia from 2016 to 08Nov2018, digoxin at 0.125 mg alternate day orally taken for heart failure from 2016 to 08Nov2018, acetylsalicylic acid (ASPIRIN) 100 mg once daily orally taken for hypertension from 2016 to 18Nov2018, calcitriol (ROCALTROL) at 0.25mg once a day orally taken for kidney failure from 2016 to 08Nov2018, amlodipine at 10 mg daily (2x5mg) orally taken for hypertension from 2016 to 08Nov2018. The subject experienced myocardial infarction on 08Nov2018 and was hospitalized. As a consequence of complication, the subject developed pulmonary edema, a shock condition, and then died. The subject died on 18Nov2018. Cause of death was complication of myocardial infarction. An autopsy was not performed. The reported SAE term was "myocardial infarction" with onset date 08Nov2018, serious criterion was hospitalization, life threatening and death. Hospitalization for the event myocardial infarction was from 08Nov2018 to 18Nov2018. The subject underwent lab tests and procedures which included coronography on 08Nov2018 with no result provided; hemoglobin was 115g/l on 08Nov2018 and 100 g/l on 15Nov2018 (normal range 130-180); WBC on 08Nov2018 was18.1 x10 9/l (normal range 0.47-0.57); creatinine was 456 umol/l on 08Nov2018, 882 umol/l on 14Nov2018 and 546 umol/l on 17Nov2018 (normal range 71-115); hematocrit on 08Nov2018 was 33.8 % (normal range 37-54), ECG readings: sinuous rythm, CT elevated in frontal wall, V1-V3 consumption; Troponin I and T: 1021.5 pg/ml, 2615.4 pg/ml, over 26358 pg/ml, 24799.6 pg/ml Angiography: 08Nov2018: no complications, 18Nov2018: no complications. The subject started dialysis on 14Nov2018. Type of dialysis reported as none (pre -dialysis). The subject did not have exposed any other erythropoietin stimulating agent (ESA). The subject did not experience any thromboembolic event during treatment with any other ESA. Therapy included nintronal 2 ml/h, 5 ml/h, 1 ml/h, 3 ml/h, heparin in therapeutic dose, furantil 5 amp/2h, 2x2t, 3 amp, 2x2 amp, 3 amp, 6 amp, 6 amp, 3+3 amp, 2x5 amp, brilique 180 mg substituted with clopidorgel 1 t, aspirin 300 mg, 100 mg, atorvastatin 40 mg, famotidine 2x20 mg substituted with pantoprazole 2x20 mg, potassium chloride 2x1 amp/12h, medocef 2x2gr, urbazone 40 mg, physiological serum 2x1b, trifas 2x100 mg, 2x50 mg, 2x20mg Retacrit 3000UI, milurit 100 mg, Norvasc 5 mg, Betaloc zoc 25 mg. The action taken in response to the event for epoetin zeta was considered as not applicable. The outcome of the event was fatal.

The investigator assessed the event myocardial infarction was unrelated to the study medication and concomitant drugs.

Follow-up (21Nov2018): New information reported includes new lab tests added, death information provided, death provided as additional serious criterion for the SAE "myocardial infarction".

Follow-up (28Nov2018): New information included: stop date of Epoetin Zeta (07Nov2018), new medical history (Ischaemic heart disease), hospitalization details (from 08Nov2018 to 18Nov2018), life threatening criterion provided for the event, concomitant details, lab tests, therapy and subject clinical course.

No follow-up activities necessary. No further information expected.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event myocardial infarction was related to the epoetin zeta. The event was most likely due to the subject's underlying cardiovascular diseases.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Activated partial thromboplastin time	38 s	
2		Activated partial thromboplastin time	99.03 %	
3		Activated partial thromboplastin time	53.1s	
4		Activated partial thromboplastin time	43.2 s	
5		Activated partial thromboplastin time	does not clot	
6		Activated partial thromboplastin time	79.6	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7		Activated partial thromboplastin time	45.7 s	
8		Activated partial thromboplastin time	43.5 s	
9		Activated partial thromboplastin time	38.6 s	
10		Alanine aminotransferase	25 u/l	
11	08-NOV-2018	Angiocardiogram		
12	08-NOV-2018	Angiogram	no complications	
13	18-NOV-2018	Angiogram	no complications	
14		Aspartate aminotransferase	40 ul	
15		Blood bicarbonate	18.5	
16		Blood bicarbonate	27.9	
17		Blood bicarbonate	21.9	
18		Blood cholesterol	4.9 mmol/l	
19		Blood creatine phosphokinase	591 u/l	
20		Blood creatine phosphokinase	178 u/l	
21		Blood creatine phosphokinase	8.36 ng/ml	
22		Blood creatine phosphokinase	201 ng/l	
23		Blood creatine phosphokinase	34.6 ng/ml	
24		Blood creatinine	616 umol/l	115 71
25		Blood creatinine	792 umol/l	115 71
26		Blood creatinine	571 umol/l	115 71
27		Blood creatinine	687 umol/l	115 71
28		Blood creatinine	687 umol/l	115 71
29		Blood creatinine	546 umol/l	115 71
30		Blood creatinine	456 umol/l	115 71
31		Blood creatinine	882 umol/l	115 71

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
32		Blood creatinine	882 umol/l	115 71
33	08-NOV-2018	Blood creatinine	456 umol/l	115 71
34	14-NOV-2018	Blood creatinine	882 umol/l	115 71
35	17-NOV-2018	Blood creatinine	546 umol/l	115 71
36		Blood culture	aaerobic	
37		Blood gases	-1.3	
38		Blood gases	90.3 %	
39		Blood gases	0.1 mmol/l	
40		Blood gases	0.6 mmol/l	
41		Blood gases	-6 mmol/l	
42		Blood gases		
43		Blood gases	94.6 %	
44		Blood gases	75.3 %	
45		Blood gases	below 0.010 mg/ml	
46		Blood glucose	11 mmol/l	
47		Blood glucose	6.2 mmol/l	
48		Blood potassium	4.2	
49		Blood potassium	4.3	
50		Blood potassium	4.1	
51		Blood potassium	3.84	
52		Blood potassium	4.2	
53		Blood potassium	3.79	
54		Blood sodium	140 mmol/l	
55		Blood sodium	137 mmol/l	
56		Blood sodium	139 mmol/l	
57		Blood sodium	140 mmol/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
58		Blood sodium	141 mmol/l	
59		Blood sodium	139 mmol/l	
60		Blood test	24.8 mmol/l	
61		Blood test	24.8 mmol/l	
62		Blood test	20.1 mmol/l	
63		Blood triglycerides	1 mmol/l	
64		Blood urea	21.5 mmol/l	
65		Blood uric acid	535 umol/l	
66		C-reactive protein increased	negative	
67		CSF culture	105 mmol/l	
68		CSF culture	104 mmol/l	
69		CSF culture	107 mmol/l	
70		CSF culture	107 mmol/l	
71		Carbon dioxide	19.5	
72		Carbon dioxide	29.5	
73		Carbon dioxide	22.8	
74		Echocardiogram	Core 32 mm...	
75		Electrocardiogram	sinous rythm, CT elevated...	
76		HIV antibody	negative	
77		Haematocrit	0.338 l/l	
78		Haematocrit	0.275l/L	
79	08-NOV-2018	Haematocrit	33.8 %	54 37
80		Haemoglobin	100 g/l	180 130
81		Haemoglobin	115 g/l	
82	08-NOV-2018	Haemoglobin	115 g/l	180 130
83	15-NOV-2018	Haemoglobin	100 g/l	180 130

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
84		Hepatitis B surface antigen	negative	
85		Hepatitis C RNA	negative	
86		High density lipoprotein	1.63 mmol/l	
87		International normalised ratio	0.9	
88		Low density lipoprotein	2.8 mmol/l	
89		Mean cell haemoglobin	33.1 pg	
90		Mean cell haemoglobin	32.2 pg	
91		Mean cell haemoglobin concentration	341.0 g/l	
92		Mean cell haemoglobin concentration	365 g/l	
93		Mean cell volume	90.8 fL	
94		Mean cell volume	94.2 fL	
95		Mean platelet volume	8 fL	
96		Mean platelet volume	9.7	
97		Oxygen saturation	18.4	
98		Oxygen saturation		
99		PCO2	53.2 mmHg	
100		PCO2	27.4 mmHg	
101		PCO2	32.5 mmHg	
102		PO2	44 mmHg	
103		PO2	52 mmHg	
104		PO2	75 mmHg	
105		Platelet count	266 x10 9/l	
106		Platelet count	272 x10 9/l	
107		Platelet distribution width	13.6 fL	
108		Platelet distribution width	11.2 fL	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
109		Platelet-large cell ratio	17 %	
110		Platelet-large cell ratio	25.8 %	
111		Procalcitonin	0.21 %	
112		Procalcitonin	0.26 %	
113		Red blood cell count	30.3 x10^12/l	
114		Red blood cell count	3.58 x10^12/l	
115		Red cell distribution width	65.4 fl	
116		Red cell distribution width	72.5 fL	
117		Red cell distribution width increased	14.4 %	
118		Red cell distribution width increased	15.1 %	
119		Syphilis	negative	
120		Troponin	over 26358 pg/ml	
121		Troponin	24799.6 pg/ml	
122		Troponin	2615.4 pg/ml	
123		Troponin	1021.5 pg/ml	
124		Urine analysis	WITHOUT GROWTH	
125		White blood cell count	15.5 x10 9/l	0.57 0.47
126		White blood cell count	18.1 x10 9/l	0.57 0.47
127	08-NOV-2018	White blood cell count	18.1 x10 9/l	0.57 0.47
128		pH body fluid	7.36	
129		pH body fluid	7.51	
130		pH body fluid	7.32	

13. Relevant Tests

ECG readings(unspecified date): sinuous rythm, CT elevated in frontal wall, V1-V3 consumption
Echocardiogram(unspecified date): Arterial core 32 mm : artery 15 mm, LP44/51/50mm, TDR 65mm, TSR: 49mm: FI 45%, ESLK 13 mm, Septum 9 mm, basal spetum: 14 mm, RC 26 mm,: RV: 39/40mm, Pericaridia - no pericardial leaks. Conclusion: LV - dilated, LC - dilated, hypokinesis, lowered pump fraction with IF 45%/ RC with normal opening, hyperkinetic, slight calcification of arterial valve. Arterial stenosis with peak gradient 33m. peak velocity 2.9 m/s. Tricuspid insufficiency 1st grade. PASN 45-50 mm. VCI 16 mm. Nullmonate blood flow - 0.36 m/s. No pericardial leaks.
ECG(08Nov2018): No complications. Conclusions: Right circulation. LM - 70 degree distal stenosis. LAD 70% ostoi - proximal

ADDITIONAL INFORMATION

13. Relevant Tests

stenosis. 99% stenosis in central segment with [illegible] blood to peryferia. LCx - no stenosis. OM1 - 85% ostoi - proximal stenosis. RCA - prolonged stenosis up to 50% in central segment. Indication for PCI of LAD: catheter EBU 3.5/6F positioned in LM. Coronary stent Terumo Runthrough located lateraly in the artery. Second stent BMW located lateraly in LCx. Unconctroled predilatation with SeQuent balloon 2.50/10mm/12atm in the area of LAD stenosis and followed by unsuccessfuul attempt at stent implantation Coroflex Isar /DES/ 3.0/13 mm. Suboptimal indirect angiology resultate, TIMI III heamorhage. Comment: Patient with OMI and multiple KB. After BCC /ventricular fibrillation/. Accomplished rescue PCI+POBA in LAD. Unsuccessful stent implantation due to turbulence and calcification. Directed to AKB.
ECG(18Nov2018): No complications. Conclusions: LM - 70% distal stenosis. LAD 70% osteaproximal stenosis, 99% stenosis in central segment. Slightly slowed blood flow. LCx - no stenosis. OM1 85% osteaoproximal stenosis. RCA - long 50% stenosis in central segment. Comment: Directed for cardiology visit for revascularisation type definitione.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	6000 IU, (3x2000) weekly; Subcutaneous	renal anemia (Nephrogenic anaemia)	MAR-2018 / 07-NOV-2018; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
NOV-2014 to Ongoing	Relevant Med History	Kidney polycystic (Congenital cystic kidney disease);
02-FEB-2016 to Ongoing	Relevant Med History	Anemia (Anaemia);
Unknown	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);

TABLE OF CONTENTS

15.3.12.2.1 Serious Adverse Event of Special Interest Narratives

Narratives are provided for serious adverse events of special interest:

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
Bg-001-0024*	2574411	Myocardial infarction
Bg-001-0048*	2016495673	Ischaemic stroke
Bg-004-0004*	2400201	Ischaemic stroke
Bg-004-0017	2896188	Peripheral artery thrombosis
Bg-004-0022	2846883	Myocardial infarction; Embolism
Bg-004-0038	2016536977	Ischaemic stroke
Bg-004-0041*	2016403477	Myocardial infarction
Bg-004-0094*	2018473550	Myocardial infarction
Bg-004-0095	2018166584	Ischaemic stroke
Bg-006-0039*	2017489626	Cerebrovascular accident
Bg-014-0002*	2085987	Acute myocardial infarction; Pulmonary embolism
Bg-014-0003*	2939556	Myocardial infarction
Bg-014-0004*	2327613	Ischaemic stroke
Bg-014-0025	3248197	Deep vein thrombosis
Bg-014-0026	3194650	Venous thrombosis
Bg-015-0017*	3181623	Cerebrovascular accident
Bg-025-0011*	2017495875	Myocardial infarction
Bg-025-0014	2017502404	Myocardial infarction
Cr-005-0001	2017202601	Cerebrovascular accident
Cr-005-0002*	2017098040	Myocardial infarction
Cr-005-0007	2017097815	Cerebrovascular accident
Cr-005-0014*	2016267631	Subdural haematoma
Cr-009-0003	3157227	Cerebral haemorrhage
Cr-009-0009	3082071	Acute myocardial infarction; Embolism
Cr-009-0010	2017468071	Cerebral infarction
Cr-012-0001	2017204715	Thrombosis
Es-024-0025*	2999144	Acute myocardial infarction
Es-024-0038*	2017447054	Acute myocardial infarction
Es-046-0003	2091030	Cerebrovascular accident
Es-051-0037	2018439471	Arteriovenous fistula thrombosis
Es-051-0046	2019134687	Arteriovenous fistula thrombosis
Es-053-0003	2019143957	Acute myocardial infarction
Es-053-0009	2019143892	Pulmonary thrombosis
Fin-001-0002*	3137952	Myocardial infarction
Fin-001-0005	2016557897	Drug ineffective
Fin-002-0002	2663539	Transient ischaemic attack
Fin-002-0003	2335062	Ischaemic stroke

Fin-008-0002	1291693	Acute myocardial infarction
Fin-008-0002	1885798	Acute myocardial infarction
Fr-064-0019*	1685920	Cerebrovascular accident
Ge-012-0007*	892943	Cerebrovascular accident
Ge-012-0017*	1891763	Cerebrovascular accident
Ge-012-0022*	1891768	Thrombosis in device
Ge-012-0070	2019210884	Acute myocardial infarction
Ge-012-0071	2017545676	Cerebrovascular accident
Ge-012-0075	2019210942	Acute myocardial infarction
Ge-012-0075	2019210970	Peripheral arterial occlusive disease
Ge-012-0080	2019210839	Acute myocardial infarction
Ge-027-0010	1232463	Cerebrovascular accident
Ge-027-0024	1647075	Cerebrovascular accident
Ge-027-0028*	1897663	Myocardial infarction
Ge-046-0005	1915772	Myocardial infarction
Ge-046-0010	1837497	Acute myocardial infarction
Ge-048-0014	1940657	Acute myocardial infarction
Ge-048-0037	2963426	Basal ganglia haemorrhage
Ge-048-0038	2017082349	Pelvic venous thrombosis
Ge-048-0041*	2018308638	Cerebral haemorrhage
Ge-069-0009	2018371605	Cerebral infarction
Ge-069-0010*	2960188	Cerebrovascular accident
Ge-069-0010*	2018371800	Infarction
Ge-083-0006*	1793228	Pulmonary embolism; Infarction
Ge-083-0008*	2400258	Cerebrovascular accident; Thrombosis
Ge-093-0045	2430832	Embolism
Ge-093-0045	2016363748	Acute myocardial infarction
Ge-093-0056	3033104	Acute myocardial infarction
Ge-093-0057	2207374	Deep vein thrombosis; Pulmonary embolism
Ge-093-0076	2971062	Acute myocardial infarction
Ge-093-0079	3024253	Thrombosis
Ge-093-0082	2016428437	Cerebral infarction
Ge-093-0085*	2400091	Cerebral infarction; Cerebral ischaemia
Ge-093-0107	2753000	Deep vein thrombosis
Ge-093-0109	2753008	Acute myocardial infarction
Ge-093-0131	3158413	Subclavian vein thrombosis
Ge-093-0131	2018023333	Thrombophlebitis superficial
Ge-093-0131	2018023245	Pelvic venous thrombosis
Ge-093-0138	3194713	Thrombosis; Acute myocardial infarction
Ge-093-0141	2018023376	Acute myocardial infarction
Ge-093-0175	2017103232	Pulmonary embolism

Ge-093-0176	2017103352	Transient ischaemic attack
Ge-093-0182	2019328714	Peripheral arterial occlusive disease
Ge-093-0185	2017269786	Coronary artery thrombosis
Ge-093-0209	2019145681	Acute myocardial infarction
Ge-094-0018	2017064878	Acute myocardial infarction
Ge-094-0018	2017414119	Cerebrovascular accident
Ge-094-0019	2017064895	Cerebral haemorrhage
Ge-094-0020	2017546018	Acute myocardial infarction
Ge-094-0023	2016562333	Transient ischaemic attack
Ge-094-0027	3234236	Myocardial infarction
Ge-094-0032*	2017435221	Myocardial infarction
Ge-094-0039	2018357453	Deep vein thrombosis
Ge-097-0013	2184107	Peripheral arterial occlusive disease
Ge-097-0020	1614917	Peripheral arterial occlusive disease
Ge-097-0024	2017248969	Cerebellar infarction; Ischaemic stroke
Ge-097-0024	2018117299	Cerebral haemorrhage
Ge-097-0024	2018117300	Intracardiac thrombus
Ge-097-0038	2019193578	Embolism
Ge-109-0003*	2820900	Acute myocardial infarction
Ge-115-0001	1393463	Cerebrovascular accident
Ge-115-0015*	998219	Arterial thrombosis
Ge-115-0031	1393560	Transient ischaemic attack
Ge-115-0035	1393630	Shunt thrombosis
Ge-115-0045	2017095389	Iliac artery occlusion
Ge-115-0092	2721395	Transient ischaemic attack
Ge-115-0102	3079051	Acute myocardial infarction
Ge-115-0112	2017073945	Embolic stroke
Ge-115-0124	2017095459	Acute myocardial infarction
Ge-115-0219	2017437944	Myocardial infarction
Ge-117-0009	2562115	Acute myocardial infarction
Ge-142-0026	2595685	Deep vein thrombosis; Pulmonary embolism
Ge-146-0003*	2052813	Acute myocardial infarction; Cerebrovascular accident
Ge-151-0001	1857083	Cerebrovascular accident; Thrombosis
Ge-152-0025*	2651469	Myocardial infarction; Cerebral infarction
Ge-158-0002	1357498	Peripheral arterial occlusive disease
Ge-165-0002	2294363	Acute myocardial infarction; Embolism
Ge-165-0006	2550831	Cerebral ischaemia
Ge-165-0006	2018029611	Cerebrovascular accident
Ge-165-0007	2117697	Acute myocardial infarction
Ge-165-0010	3154886	Embolism
Ge-165-0010	2016534792	Cerebral infarction

Ge-432-0001	2735896	Acute myocardial infarction
Ge-432-0004	2126673	Acute myocardial infarction; Cerebral ischaemia; Embolism
Ge-432-0005	1595758	Acute myocardial infarction
Ge-432-0015	2131955	Retinal infarction; Acute myocardial infarction
Ge-432-0020	2017389668	Peripheral embolism
Ge-454-0018*	2817079	Myocardial infarction
Ge-454-0042	2016542530	Acute myocardial infarction
Ge-463-0008*	2021971	Basal ganglia haemorrhage; Subdural haematoma
Ge-463-0015*	2233652	Myocardial infarction
Ge-471-0015*	2715463	Pulmonary embolism
Ge-471-0016*	2016459865	Myocardial infarction
Ge-471-0033*	2016583774	Myocardial infarction
Ge-471-0041	2016401625	Cerebrovascular accident
Gr-002-0019*	2693195	Acute myocardial infarction
Gr-002-0025*	2797025	Myocardial infarction
Gr-003-0012*	2453067	Myocardial infarction
Gr-003-0024	2819938	Cerebrovascular accident
Gr-013-0002*	2016295847	Acute myocardial infarction; Embolism
Gr-017-0009	2618581	Acute myocardial infarction
Gr-031-0004*	2411460	Myocardial infarction
Gr-034-0009*	2017358130	Myocardial infarction
Gr-034-0010*	2017358127	Cerebrovascular accident
Gr-045-0026*	2737056	Pulmonary embolism
Gr-045-0051*	2018212348	Myocardial infarction
Gr-051-0005*	2602755	Myocardial infarction
Gr-051-0024*	3084735	Embolism
Gr-051-0031*	2605484	Myocardial infarction
Gr-051-0041	2880827	Embolism; Cerebrovascular accident
Gr-051-0085*	2017253323	Myocardial infarction
Gr-051-0090*	2017244407	Myocardial infarction
Gr-052-0006*	2965870	Cerebrovascular accident
Gr-052-0010*	3168514	Cerebral haemorrhage
Gr-059-0006*	2018036059	Myocardial infarction
Gr-062-0006*	3073610	Cerebrovascular accident
Gr-065-0005*	3272375	Myocardial infarction
It-022-0015	2519067	Acute myocardial infarction
It-022-0018	2481084	Embolism
It-038-0002	1438497	Ischaemic stroke
It-038-0014*	1391691	Haemorrhagic stroke
It-059-0009	2018031606	Acute myocardial infarction

It-073-0027	2018413068	Deep vein thrombosis
It-084-0001	1206113	Myocardial infarction
It-087-0004	1617854	Drug ineffective
It-090-0022*	2791899	Cerebral haemorrhage
It-093-0005*	2069922	Cerebrovascular accident
It-116-0018*	2016281626	Myocardial infarction
It-116-0021*	2649763	Acute myocardial infarction
It-116-0022	2899611	Drug ineffective
It-116-0024*	2789600	Cerebrovascular disorder
It-116-0032	2876300	Aplasia pure red cell; Drug ineffective
It-120-0019*	2653522	Cerebrovascular accident
It-120-0033*	2018006285	Acute myocardial infarction
Sw-005-0001	2706487	Pulmonary embolism
Sw-005-0002*	1402439	Myocardial infarction
Sw-005-0002*	2139224	Myocardial infarction
Sw-005-0014*	2188609	Myocardial infarction
Sw-005-0025	3023456	Myocardial infarction
Sw-005-0025	2016461859	Acute myocardial infarction
Sw-005-0028	3023465	Myocardial infarction
Sw-005-0030	2830712	Acute myocardial infarction
Sw-005-0031	2893017	Cerebral haemorrhage
Sw-005-0039*	3291130	Acute myocardial infarction
Sw-005-0040	3214713	Acute myocardial infarction; Transient ischaemic attack
Sw-005-0040	2017001948	Pulmonary embolism
Sw-005-0041	3023485	Embolic cerebral infarction
Sw-005-0051	2017448837	Myocardial infarction
Sw-011-0007	2195433	Myocardial infarction
Sw-011-0023*	2016443936	Myocardial infarction
Sw-011-0028*	2018182041	Cerebral haemorrhage
Sw-011-0028*	2018213835	Cerebrovascular accident
Sw-011-0045	2019431417	Acute myocardial infarction
Sw-018-0003*	1550791	Myocardial infarction
Sw-018-0008*	2819992	Myocardial infarction; Transient ischaemic attack
Sw-018-0012	2653063	Myocardial infarction

This clinical trial report contains narratives printed in a CIOMS format with a "Draft" watermark. This watermark signifies that these narratives were not produced for the submission of individual case safety reports to a regulatory agency. These narratives contain the information available in the safety database as of 27-Aug-2020 and are considered final.
*Narrative for these patients appear in Section 15.3.12.1– Death Narratives.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Fin-008-0002

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 1291693, 1885798

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Acute myocardial infarction (AER# 1291693)	AMI
Acute myocardial infarction (AER# 1885798)	Acute myocardial infarction
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Causes of Death:	
Organ failure	Organ failure
Pneumonia	Pneumonia

This 87-year-old White male patient was enrolled in post-authorization safety cohort observation study on 05 Mar 2012 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of renal failure (since 17 Mar 1997); renal cancer (since 22 Mar 1997); and hypertensive nephropathy, hypertension, and venous embolism (all since unknown dates).

The patient began dialysis 2 times per week from 14 Sep 2010, and he started receiving SC epoetin zeta at a total dosage of 114 IU/kg/week (2 dosage/week) from 28 Sep 2010. Concomitant medications included calcium carbonate, acetylsalicylic acid, and ascorbic acid/biotin/calcium pantothenate/folic acid/nicotinamide/pyridoxine hydrochloride/riboflavin/thiamine mononitrate.

On 11 May 2012 (Study Day 68), two days after receiving a dose of epoetin zeta, the patient was diagnosed with a reported event of AMI (MedDRA preferred term [PT]: acute myocardial infarction-first occurrence), which was a life-threatening event resulting in hospitalization on the next day (Study Day 69). The patient was treated with an unspecified non-invasive treatment. It was reported that the patient was not exposed at any time to any other erythropoietin-stimulating agent. The action taken with epoetin zeta in response to the event was not reported. On an unknown date, the patient recovered from acute myocardial infarction (first occurrence) and was discharged from the hospital on 26 May 2012 (Study Day 83).

On 14 Jul 2013 (Study Day 497), two days after receiving a dose of epoetin zeta, the patient again experienced a reported event of acute myocardial infarction (MedDRA PT: acute myocardial infarction - second occurrence), which was a life-threatening event resulting in hospitalization. The patient was treated with non-invasive treatment for the event. Action taken with epoetin zeta in response to the event was unknown. On an unknown date, the patient recovered from the event, and was discharged from the hospital on 26 Jul 2013 (Study Day 509).

On an unknown date, the patient was diagnosed with organ failure and pneumonia; treatment for these events was not reported. On 25 Nov 2013 (Study Day 631), the patient died due to organ failure and pneumonia. It was not reported if an autopsy was performed. Organ failure and pneumonia resulting in death was reported as not related to epoetin zeta.

In the opinion of the Investigator, there was not a reasonable possibility that the events of acute myocardial infarction were related to epoetin zeta. The Sponsor concurred with this assessment that the reported events of acute myocardial infarction were not related to epoetin zeta.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-012-0075

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2019210942, 2019210970

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Acute myocardial infarction (AER# 2019210942)	NSTEMI
Peripheral arterial occlusive disease (AER# 2019210970)	PAVK
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	Unknown

This 73-year-old White male patient was enrolled in post-authorization safety cohort observation study on 18 Apr 2016 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of renal failure (since 19 Dec 2005); and diabetic nephropathy, atrial fibrillation, coronary artery disease, type 2 diabetes mellitus, hyperlipidemia, hypertension, and myocardial infarction (all since unknown dates).

The patient was not on dialysis and did not receive any prior erythropoiesis stimulating agent. The patient started receiving SC epoetin zeta at a total dosage of 32 IU/kg/week (1 dosage/week) from 18 Apr 2016 (Study Day 1). No concomitant medications were reported.

On 10 Nov 2016 (Study Day 207), the patient was diagnosed with a reported event of NSTEMI (MedDRA preferred term [PT]: acute myocardial infarction), which was a life threatening event resulting in hospitalization on an unknown date. No action was taken with epoetin zeta in response to the event. No treatment was reported for the event. On 15 Nov 2016 (Study Day 212), the event of acute myocardial infarction resolved and the patient was discharged from the hospital on an unknown date.

On 10 Jan 2017 (Study Day 268), the patient experienced a reported event of PAVK (MedDRA PT: peripheral arterial occlusive disease) which was considered to be an important medical event requiring medical or surgical intervention. No action was taken with epoetin zeta in response to the event. It was reported that an outpatient examination was arranged for the patient; however, no further details were reported. No investigations or treatment was reported for the event. The event was considered resolved on the same day of onset (Study Day 268).

In the opinion of the Investigator, there was not a reasonable possibility that the events of acute myocardial infarction and peripheral arterial occlusive disease were related to epoetin zeta or concomitant medications. Per Sponsor, based on the compatible temporal association and the drug's known safety profile, the company could not completely exclude a causal relationship between the non STEMI and suspect drug epoetin zeta. The Sponsor concurred with Investigator's assessment that the event of peripheral arterial occlusive disease was not related to epoetin zeta. According to the Sponsor, the event of peripheral arterial occlusive disease was more likely due to underlying or inter-current medical conditions.

On 12 Oct 2018 (Study Day 908), the patient died. The cause of death was not reported.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-093-0045

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2430832, 2016363748

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Embolism (AER# 2430832)	Thromboembolic events
Acute myocardial infarction (AER# 2016363748)	NSTEMI
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Cause of Death:	Not applicable

This 49-year-old White male patient was enrolled in post-authorization safety cohort observation study on 01 Jul 2013 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of drug (cefazolin and mivacurium) hypersensitivity (on unknown date), congenital cystic kidney disease, coronary artery disease, hyperlipidemia, hypertension, myocardial infarction, peripheral arterial occlusive disease, myocardial ischemia, and atrial fibrillation (all since unknown dates); and renal failure (since 2004). The patient's prior surgeries included femorofemoral crossover bypass (in June 2002), implantation of aortic bifemoral Y-bypass (in April 2005), coronary bypass surgery (in November 2007), thromboendarterectomy of internal carotid artery left sided (in March 2009), femoral Dacron bypass left-sided (in May 2009), 3-fold drug eluting stent (DES) in posterior cerebral artery (in September 2009), popliteal-crural extension of bypass (in January 2010), thromboendarterectomy in popliteal artery, creation of a prothesio-popliteal Dacron bypass, a prothesio-profundal Dacron bypass and a popliteo-popliteal bypass right-sided (in March 2010), renewed insertion of DES (in July 2010), creation of iliaco-obturator bypass right-sided (in August 2010), implantable cardioverter defibrillator (ICD) insertion (on 23 Aug 2012), and coronary angiography (in September 2012). The patient was a current smoker; and underwent right leg amputation due to peripheral arterial occlusive disease on 11 Nov 2015.

The patient began dialysis 3 times per week from 23 Jul 2007, and received prior darbepoetin alfa 727.3 ng/kg/week from 01 Jul 2008, epoetin zeta (Silapo) at 4000 IU/week from 13 Sep 2010 to 18 May 2011, epoetin alpha (Abseamed) at 12000 IU/week from 20 May 2011 to 21 May 2013, and epoetin theta (Biopoin) at 5000 IU/week from 31 May 2013 to 28 Jun 2013. The patient started receiving SC epoetin zeta at a total dosage of 145.5 IU/kg/week (3 dosage/week) from 01 Jul 2013 (Study Day 1). It was reported that

the patient did not experience any thromboembolic event during treatment with any other erythropoietin stimulating agents. No concomitant medications were reported.

On an unknown date, the patient experienced a reported event of thromboembolic events (MedDRA preferred term [PT]: embolism), which was considered as a medically significant event requiring medical or surgical intervention. Action taken with the epoetin zeta in response to the event and the treatment given and outcome of the event of embolism were reported as unknown.

On 20 Feb 2016 (Study Day 965), one day after receiving a dose of epoetin zeta, the patient was diagnosed with a reported event of NSTEMI (MedDRA PT: acute myocardial infarction) and was hospitalized. On the same day, the patient's electrocardiogram showed sinus rhythm with a heart rate of 80 beats per minute with no elevations or depressions. A transthoracic echocardiography showed sclerosed aortic and mitral valves (posterior mitral leaflet), without relevant cardiac defects and implied inferior hypokinesis. Normal wide ventricles and atria, normal global systolic left ventricular function, and no significant pericardial effusion were observed. It was reported that the patient started to suffer from increasing angina pectoris complaints responding to nitroglycerin (Class 3-4 according to Canadian Cardiovascular Society grading of angina pectoris) for the past 4 days. Since the previous bypass surgery, he had been experiencing intermittent load-dependent angina pectoris complaints, but the pain was not that intense as now, nor had it ever appeared in rest. On the same day of admission, the patient underwent dialysis. Within the frame of dialysis, cardiac enzymes were checked. The results showed distinctly increased levels of blood creatine phosphokinase, myocardial necrosis marker, and troponin (the values are not reported). During admission, the patient was clinically in a stable condition with no afflictions, no elevations to see in ECG. During further course, the patient suffered from persistent angina pectoris. The action taken with epoetin zeta in response to the event of acute myocardial infarction was unknown.

On 22 Feb 2016 (Study Day 967), a coronary angiogram revealed coronary artery disease (3-vessel disease); and a percutaneous coronary intervention with implantation of a drug eluting stent was performed. On the same day, the patient received dialysis, but this had to be interrupted due to the pain in the area of the shunt. On 23 Feb 2016 (Study Day 968), the patient underwent dialysis initially and subsequently, returned back to the convalescent home for triple therapy with phenprocoumon, clopidogrel, and acetylsalicylic acid according to current recommendations due to atrial fibrillation and recent stent implantation. These drugs should be administered for about 4 weeks initially, followed by treatment with clopidogrel and phenprocoumon for about 11 months. On the same day (Study Day 968), the patient recovered from the event of acute myocardial infarction and was discharged from the hospital. Discharge medications included acetylsalicylic acid, clopidogrel, phenprocoumon, alfacalcidol, omeprazole, atorvastatin, ezetimibe, irbesartan, bisoprolol, furosemide, amitriptyline, calcium acetate, ranolazine, and isosorbide dinitrate.

On 22 Jul 2016 (Study Day 1118), the patient completed the study.

The Investigator causality assessment for the event of embolism in relation to epoetin zeta was not reported. The Sponsor considered that event of embolism was possibly related to

epoetin zeta. Per Sponsor, the multiple cardiovascular risk factors in the medical history, could not provide a more definitive causality assessment without firm timeline and objective clinical event details on the reported event of thromboembolic event.

The Investigator causality assessment for the event of acute myocardial infarction to epoetin zeta was reported as not assessable. The Sponsor considered that there was not a reasonable possibility that the event of acute myocardial infarction (NSTEMI) was related to epoetin zeta. According to the Sponsor, the patient's medical history of hyperlipidemia, ischemic heart disease, and atrial fibrillation might provide plausible explanations for the event.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-093-0131

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 3158413, 2018023333, 2018023245

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Subclavian vein thrombosis (AER# 3158413)	Thrombosis of vena subclavia right side
Thrombophlebitis superficial (AER# 2018023333)	Thrombosis of vena femoralis superfacialis left side
Pelvic venous thrombosis (AER# 2018023245)	Thrombosis of vena iliaca right side
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	Unknown

This 82-year-old White male patient was enrolled in post-authorization safety cohort observation study on 13 Jul 2015 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of esophageal anastomosis and esophageal mucosal dissection (both on unknown date); cerebrovascular disorder, myocardial ischemia, coronary artery disease, hypertension, hypertensive nephropathy, Parkinson's disease, right inguinal hernia, venous thrombosis limb, atrioventricular block second degree, cardiac pacemaker insertion, dementia, chronic obstructive pulmonary disease, and atrial fibrillation (all since unknown dates); esophageal carcinoma (since 2006); and renal failure (since 17 Nov 2014). The patient also had Demers catheter via the vena subclavian on the right side; and installment of dialysis shunt (on 26 Aug 2015); and penile cancer (penis amputation and scrotal plastic in 13 Dec 2016).

The patient began dialysis 3 times per week from 17 Nov 2014, and he started receiving SC epoetin zeta from 21 Nov 2014 at a total dosage of 160 IU/kg/week (3 dosage/week). The patient was not treated with any other erythropoiesis-stimulating agent before treatment with epoetin zeta. Concomitant medications included allopurinol, omeprazole, metamizole, phenprocoumon, pantoprazole sodium sesquihydrate, alfacacidol, and loperamide hydrochloride.

On 16 Sep 2015 (Study Day 66), on the day after receiving a dose of epoetin zeta, the patient experienced a reported event of thrombosis of vena subclavia right side (MedDRA preferred term [PT]: subclavian vein thrombosis) and was admitted to hospital. It was reported that the

patient had severely swollen arm due to the subclavian vein thrombosis on the left side in the presence of the cubital shunt on the left side. Action taken with epoetin zeta in response to the event of subclavian vein thrombosis was unknown. Treatment included cancellation of dialysis shunt reported as closure of the cubital shunt with separation and suture near the anastomosis, compression bandage, and administration of heparin and cefuroxime. On 21 Sep 2015 (Study Day 71), the patient was discharged from the hospital. At the time of discharge, the patient had not recovered from the event and the wound healing was progressing normally and by first intention. The patient was recommended for regular wound checks and the removal of the introduced suture materials on the tenth postoperative day; disinfectant flushing, an absorbent compression bandage, an arm compression sleeve; and a home care service was arranged. Treatment with heparin and oral antibiotics (unspecified) was indicated for another 7 days, and vitamin K antagonists was recommended for at least 3 months; and another consultation was requested to check the findings at the vascular surgery outpatient department in 10 days.

On 28 Jul 2016 (Study Day 382), the patient underwent insertion of Demers catheter via right external iliac vein, and he had a previous Demers infection in April 2017. He was diagnosed with coagulation disorder (coagulopathy) after coagulation lapse under phenprocoumon in May 2017.

On 05 Jul 2017 (Study Day 724), two days after receiving a dose of epoetin zeta, the patient was admitted to the hospital due to Methicillin-sensitive *Staphylococcus aureus* (MSSA)-sepsis associated with Demers-catheter infection and Morbus Parkinson. On the same day, the patient was diagnosed with a reported event of thrombosis of vena femoralis superfacialis left side (MedDRA PT: thrombophlebitis superficial). The laboratory investigations revealed international normalized ratio (INR) of 1.96 (normal range [NR]: 0.86 to 1.0) and a prothrombin time of 40% (NR: 70% to 130%), blood creatinine phosphokinase of 267 IU/L (NR: <174 IU/L), and a blood culture was positive for MSSA. It was reported that the patient's general condition was worsening and he had mild increase of infection. At admission, the physical examination revealed that the patient was conscious, stable but reduced general condition and moderate supernutrition. The patient had tachypnea, tachycardia, and middle blistered crepitation on left side. He had mild peripheral edema with no signs of deep vein thrombosis. A Duplex sonography of both lower extremities showed complete thrombosis at upper leg area, superficial femoral vein on right side and unable to compress; deep venous system on left side from groin to distal upper leg niveau with evidence of venous flow and ability to compress. A transesophageal echocardiography showed normal systolic left ventricular (LV) function with an LV ejection fraction of 62%, sclerosis of aortic valve, mild insufficiency of mitral and tricuspid valves, and systolic PA pressure of 50 mmHg, with no evidence of vegetation or mobile structures at native valves and pacemaker tubes. The patient was treated with piperacillin/tabzobactam and his L-Dopa dosage was adjusted associated with akinetic crisis. The patient's antibiotics were changed to flucloxacillin due to the presence of MSSA in multiple blood cultures. On 07 Jul 2017 (Study Day 726), a chest x-ray showed a central jam, but an additional infiltration could not be excluded, and the laboratory results showed C-reactive protein (CRP) of 2.6 mg/dL (NR: <0.5 mg/dL), INR of 2.2, prothrombin time of 33.9%, and a white blood cell count of $16.0 \times 10^3/\mu L$ (NR: 3.6 to $10.5 \times 10^3/\mu L$). No action was taken with epoetin zeta in response to the event of superficial thrombophlebitis. On 09 Jul 2017 (Study Day 728), the patient's

CRP improved to 0.8 mg/dL. The patient's general condition improved quickly. Akinetic signs of known Parkinson syndrome improved and the infection values in laboratory tests decreased. On 10 Jul 2017 (Study Day 729), the event of superficial thrombophlebitis resolved, and after a non-complicated hospital course, the patient was discharge in improved general condition.

On 23 Aug 2017 (Study Day 773), two days after receiving a dose of epoetin zeta, the patient was hospitalized due to swelling and redness of the right leg, which had been ongoing for a few days. He had mild swelling and redness of right distal lower leg with scope difference of approximately 1 cm compared with the other side. Both feet were equally warm with no hint of critical ischemia. Homan and Payr signs were negative. Doppler sonography of veins showed thrombosis of external iliac vein, common femoral vein, and distal part of superficial femoral vein on the right side. Popliteal vein had a free flow. The patient was diagnosed with a reported event of thrombosis of vena iliaca right side (MedDRA PT: pelvic venous thrombosis). At admission, the Quick value was at 14%; and the patient was treated with Marcumar. However, treatment with Marcumar was withheld due to coagulation lapse under Marcumar therapy (INR 4.14), and the patient was conservatively treated with leg elevation and staying in bed. No compression therapy was done due to the existing peripheral arterial occlusion disease. On 26 Aug 2017 (Study Day 776), the patient's INR was 1.71; and Marcumar therapy was restarted. No action was taken with epoetin zeta in response to the event of pelvic venous thrombosis. On 28 Aug 2017 (Study Day 778), the event of pelvic venous thrombosis resolved and the patient was discharged from the hospital with a Quick value of 39%.

The patient died on 18 Oct 2017 (Study Day 829). The cause of death was unknown.

The Investigator's causality between the event of subclavian vein thrombosis and epoetin zeta was not assessable. According to the Investigator, the patient's coronary artery disease, cerebrovascular disease, hypertension, esophageal cancer, and the recent surgery for installment of dialysis shunt were considered as risk factors. The Sponsor did not concur with this assessment and reported that the event of subclavian vein thrombosis was related to epoetin zeta due to temporal relation; however, the predisposing and pre-existing risk factors were also considered as an alternative explanation.

In the opinion of the Investigator, there was not a reasonable possibility that the events of superficial thrombophlebitis and pelvic venous thrombosis were related to epoetin zeta, concomitant medications, or to a clinical trial procedure. The Sponsor concurred with this assessment. According to the Sponsor, the event of superficial thrombophlebitis was considered to be more likely due to the patient's co-morbidities including paroxysmal atrial fibrillation, esophageal and penile cancers, terminal renal insufficiency, hypertension, and sepsis associated with Demers-catheter infection. According to the Sponsor, the medical history of coronary artery disease and hypertension might provide a plausible explanation for the event of pelvic venous thrombosis.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-094-0018

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2017064878, 2017414119

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Acute myocardial infarction (AER# 2017064878)	NSTEMI
Cerebrovascular accident (AER# 2017414119)	Suspected apoplexy
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	Not applicable

This 63-year-old White female patient was enrolled in post-authorization safety cohort observation study on 21 Jul 2015 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of renal failure (since March 1999), hyperlipidemia and end stage renal disease (since 24 Mar 1999), myocardial infarction (2004), hypertension (since 05 Oct 2005), cerebrovascular accident (2007), myocardial ischemia (since August 2007), coronary artery disease (since 22 Aug 2007), left renal carcinoma (diagnosed in November 2007), transient ischemic attack (on 31 Jan 2011), ovarian carcinoma of unknown origin (from 16 Jul 2013 to 28 Aug 2013), and glomerulonephritis and venous embolism (both since unknown dates).

The patient began dialysis 3 times per week from August 2009, and received prior SC epoetin theta 148 IU/kg/week from August 2010. The patient started receiving SC epoetin zeta at a total dosage of 148 IU/kg/week (3 dosage/week) on 21 Jul 2015 (Study Day 1). Concomitant medications included simvastatin, carvedilol, ascorbic acid/calcium pantothenate/folic acid/nicotinamide/pyridoxine hydrochloride/riboflavin/thiamine hydrochloride, sevelamer carbonate, sertraline, torasemide, pantoprazole, zopiclone, colecalciferol, alfacalcidol, isosorbide mononitrate, and molsidomine retard.

On 18 Jan 2017 (Study Day 548), one day after receiving a dose of epoetin zeta, the patient was diagnosed with a reported event of NSTEMI (MedDRA preferred term [PT]: acute myocardial infarction) and was hospitalized that same day. Symptomatic therapy was provided. Due to recurrent pain, a coronary catheterization was performed which revealed a three vessel disease with in-stent re-stenosis of circumflex artery. The patient underwent a percutaneous transluminal angioplasty with single drug-eluting stent implantation. The action taken with epoetin zeta in response to the event was unknown. On 30 Jan 2017

(Study Day 560), the patient recovered from the event, and was discharged from the hospital with an advice to take acetylsalicylic acid 100 mg once daily.

The patient underwent shunt-thrombectomy with change of double lumen dialysis catheter via V. jugularis on 14 Jul 2017 (Study Day 725) and 23 Aug 2017 (Study Day 765). Her risk factors included aneurysm and partial immobilization (the patient used a rollator).

On 21 Sep 2017 (Study Day 794), two days after receiving a dose of epoetin zeta, the patient had a reported event of suspected apoplexy (MedDRA PT: cerebrovascular accident) and was hospitalized. While hospitalized, a computerized tomography scan of brain was performed, which showed microangiopathy, without any fresh insult, space requirement or bleeding. An electrocardiogram showed sinus rhythm (65 beats per minute). No treatment details were reported. No action was taken with epoetin zeta in response to the event of cerebrovascular accident. On 29 Sep 2017 (Study Day 802), the patient recovered from the event, and was discharged from the hospital on an unknown date.

On 24 Jul 2018 (Study Day 1100), the patient completed the study.

In the opinion of the Investigator, there was not a reasonable possibility that the events of acute myocardial infarction and cerebrovascular accident were related to epoetin zeta or concomitant medications. The Sponsor concurred with this assessment. According to the Sponsor, the event of acute myocardial infarction was considered to be more likely due to the patient's underlying conditions of renal carcinoma, coronary heart disease, arterial hypertension, and hyperlipidemia; and the event of cerebrovascular accident was most likely due to the patient's underlying cardiovascular conditions.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-097-0024

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2017248969, 2018117299, 2018117300

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Cerebellar infarction (AER# 2017248969)	PICA cerebellum lacuna left
Ischaemic stroke (AER# 2017248969)	Brain stroke, ischemic by carotis-stenosis
Cerebral haemorrhage (AER# 2018117299)	Intracerebral bleeding
Intracardiac thrombus (AER# 2018117300)	Heart ear thrombus
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Cause of Death:	Not applicable

This 69-year-old White male patient was enrolled in post-authorization safety cohort observation study on 17 Apr 2015 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of drug (repaglinide) reaction (on an unknown date); transient ischemic attack, peripheral neuropathy, hyperuricemia, mitral value incompetence, tricuspid valve incompetence, hypothyroidism, and vitamin D deficiency (all since unknown dates); and obesity (since unknown date) with a body mass index of 31.1 kg/m^2 at study entry; atrial fibrillation and hypertension (both since 1987); type 2 diabetes mellitus (since 1992); chronic kidney disease (since 2005); hyperlipidemia (since 09 May 2005); renal failure (since 10 Nov 2011); peripheral arterial occlusive disease (since 13 Aug 2014); stent placement (in 2015); coronary artery disease and carotid artery stenosis (both since 2015); and myocardial ischemia (since 20 Mar 2015).

The patient was not on dialysis, and he received prior SC epoetin zeta from 05 Aug 2013 at 2000 IU every 2 weeks. The patient started receiving SC epoetin zeta at a total dosage of 19 IU/kg/week (1 dosage/week) from 17 Apr 2015 (Study Day 1). Concomitant medications included dihydralazine sulfate, moxonidine, ramipril, levothyroxine sodium/potassium iodide, atorvastatin calcium/ezetimibe, metoprolol succinate, amlodipine, rivaroxaban, dulaglutide, insulin glargine, repaglinide, magnesium, iodine, magnesium oxide, colecalciferol, pantoprazole sodium sesquihydrate, torasemide, enoxaparin sodium, levothyroxine, Kalimjodid, apixaban, and magnesium citrate.

On 24 Apr 2017 (Study Day 739), approximately 17 days after receiving a dose of epoetin zeta, the patient was hospitalized with a reported event of posterior inferior cerebellar artery cerebellum lacuna infarct (MedDRA preferred term [PT]: cerebellar infarction). It was reported that the patient had a motor aphasia and a slight hemiparesis on the right. The patient had an ongoing history of atrial fibrillation for many years and, since at the time of admission, therapy with low molecular weight heparin was ongoing, a cardio embolic infarction was suspected. The patient was discharged on 08 May 2017 (Study Day 753). On 10 May 2017 (Study Day 755), the patient was readmitted with a deterioration of the pre-existing hemiparesis on the right and unchanged aphasia. On the same day, a computerized tomography scan of head showed a cerebral hemorrhage, which transcended the former infarct area. Multiple fresh hemorrhages on the left in media flow area, with a secondary hemorrhaged media infarction on left. No ventricular infiltration or subarachnoid bleeding were noted. An electrocardiogram (ECG) showed frequent atrial fibrillation (89 beats per minute [bpm]). On 12 May 2017 (Study Day 757), an ECG showed bradycardia (45 bpm) and frequent atrial fibrillation.

On 15 May 2017 (Study Day 760), the patient developed a reported event of brain stroke, ischemic by carotis-stenosis (MedDRA PT: ischaemic stroke). On 16 May 2017 (Study Day 761), the patient's ECG showed atrial fibrillation with heart rate ranging between 50 to 160 bpm (average 73 bpm). The CT with contrast showed constant large lobar intracerebral bleeding left frontotemporoparietal with unchanged perilesional edema and compression of left lateral ventricle without indication of liquor circulatory disturbance, otherwise constancy of findings. A chest x-ray was unremarkable. Treatment with apixaban was immediately discontinued. In addition, there were nocturnal bradycardias with heart rates of less than 30 bpm. Hence, the antihypertensive medication was changed and moxonidine was withdrawn as a potential trigger of the bradycardia. Upon admission, there was also a slight-motor disturbance of the right hand as well as a motor-accentuate aphasia. At the time of admission, the patient was awake, oriented to all qualities, motor-accentuate aphasia with clear word-finding disorders, paraphrasia as well as phrases, and in good general condition. Neurological examination showed cranial nerves: pupils isochoric, prompt light reaction with smooth eye movements, no pathological nystagmus, facial sensitivity equal on both sides, no facial palsy; with other cranial nerves intact. Motor examination showed: normotensive eutrophic musculature, feeling of heaviness in the arm hold test and discrete pronation on the right, leg retention on both sides safe. No high grade of paresis could be detected in the individual force test. Reflexes: muscle reflexes of the upper extremities sidewise weakly triggerable, patellar reflex and Achilles tendon reflex were absent on both sides. Babinski sign was negative on both sides. Sensitivity: anesthesia and analgesia were indicated intact on both sides, hypoesthesia of both malleoli was 4/8. Coordination test: standing and walking, and the finger-nose test: safe on both sides, difficult walk tests: unsafe, knee-heel test: right-dysmetrically, and fine-motor disturbance of the right hand. There was still a moderate aphasia and apraxia of speech, and the communication in everyday life of the patient was still difficult.

Due to the continuing serious impairment and the good success so far, the continuation of speech therapy was strongly recommended. The patient was integrated into multimodal therapy, consisting of intensive speech therapy, ergotherapy, physiotherapy, medical train therapy and neuropsychology. Rehabilitation outcome: Barthel index at admission: 75/100.

Barthel-index at discharge: 100/100. Rivermead Mobility Index score was 13/15 and 14/15 at admission and discharge, respectively. During hospitalization, the patient's activated partial thromboplastin time, platelet count, and international normalized ratio were all within normal range. No action was taken with epoetin zeta in response to these events. The events of cerebellar infarction and ischaemic stroke were considered resolved with sequelae on an unknown date.

On 23 May 2017 (Study Day 768), the patient developed a reported event of intracerebral bleeding (MedDRA PT: cerebral haemorrhage) which prolonged the patient's existing hospitalization. This event was considered medically significant requiring medical or surgical intervention. The patient was treated with anticoagulation, antihypertensives, and brain training. The action taken with the epoetin zeta in response to the event was reported as unknown. The action taken with apixaban was unknown. Consequences of the stroke and the cerebral hemorrhage had almost completely regressed. The event intracerebral bleeding was considered resolved with sequelae (unspecified) on an unspecified date. On 27 Jun 2017 (Study Day 803), the patient was discharged from the hospital. The patient was discharged in stable general condition and to further outpatient treatment. At the time of discharge, the patient was able to manage medium to long distances safely without any tools, alternating with stair climbing.

On 08 Dec 2017 (Study Day 967), the patient developed a reported event of heart ear thrombus (MedDRA PT: intracardiac thrombus), which resulted in disability and hospitalization on the same day. The action taken with epoetin zeta in response to the event was unknown. The patient received unspecified treatment for the event. On an unspecified date, he recovered from the event with sequelae (unspecified). On 13 Dec 2017 (Study Day 972), the patient was discharged from the hospital.

On 16 Mar 2018 (Study Day 1065), the patient completed the study.

In the opinion of the Investigator, there was not a reasonable possibility that the events of cerebellar infarction and ischaemic stroke were related to epoetin zeta or concomitant medication. In the opinion of the Investigator, there was not a reasonable possibility that the event of cerebral haemorrhage was related to epoetin zeta but was related to apaxiban. The Sponsor concurred with this assessment. According to the Sponsor, the underlying conditions including coronary heart disease, carotid-stenosis, hypertension, hyperlipidemia, atrial fibrillation, ischemic heart disease, obesity, type II diabetes mellitus were significant risk factors in causing the reported events of cerebellar infarction and ischaemic stroke. The Sponsor reported that the event of cerebral hemorrhage was due to underlying atrial fibrillation which were significant risk factors for the ischemic brain infarction and left atrial thrombus. However, a possible contributory role of the suspect drug apixaban in the reported event could not be completely excluded given the known suspect drug profile and/or temporal association.

In the opinion of the Investigator, there was not a reasonable possibility that the event of intracardiac thrombus was related to epoetin zeta, concomitant medications or a clinical trial procedure. The Sponsor concurred with this assessment. According to the Sponsor, the

patient's medical history of type 2 diabetes mellitus, stage 3 chronic kidney disease, and coronary artery disease might provide explanations for the event.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-165-0006

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 2550831, 2018029611

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Cerebral ischaemia (AER# 2550831)	Suspicious cerebrovascular ischemia
Cerebrovascular accident (AER# 2018029611)	Apoplexy (ACM)
Drug Permanently Discontinued Due to the SAEs of Special Interest?	Unknown
Cause of Death:	Unknown

This 73-year-old White female patient was enrolled in post-authorization safety cohort observation study on 03 Dec 2012 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of prolonged immobilization (unknown date); cerebrovascular disorder, coronary artery disease, transient ischemic attack, diabetic nephropathy, and obesity (all since unknown dates); vascular malformation (angiopathy; since 08 May 2000); type 2 diabetes mellitus (since 06 Jun 2012); renal failure (since 18 Jun 2012); and hypertension and myocardial ischemia (both since 17 Nov 2012).

The patient began dialysis 3 times per week from 17 Nov 2012. The patient had not received any other erythropoietin stimulating agents. The patient started receiving SC epoetin zeta at a total dosage of 84.5 IU/kg/week (3 dosage/week) from 03 Dec 2012 (Study Day 1). Concomitant medications included acetylsalicylic acid, bisoprolol, furosemide, amlodipine, dihydralazine sulfate, pentaerithrityl tetranitrate, amitriptyline hydrochloride, simvastatin, colecalciferol, pantoprazole sodium sesquihydrate, metamizole sodium, torasemide, xipamide, carbimazole, and clopidogrel besylate.

The patient had an ongoing history of cardiac arrhythmia since April 2014. However, she was not on oral anticoagulation with Marcumar because of the age and multi morbidity CHADVAS-score.

On 14 Apr 2014 (Study Day 498), the patient suddenly was disoriented and became aggressive; however, she had no paresis of arms or legs. On the same day, the patient was hospitalized with a reported event of suspicious cerebrovascular ischemia (MedDRA preferred term [PT]: cerebral ischaemia). On an unknown date, a computerized tomogram scan of head showed no ischemia. The patient's neurologist considered possibility of an ischemic insult. The patient was treated with haloperidol and risperidone for the event of

suspicious cerebrovascular ischemia. On an unknown date, the event of suspicious cerebrovascular ischemia was considered resolving. On 15 Sep 2014 (Study Day 652), the patient experienced angina pectoris. The patient was treated with nitro spray for angina pectoris with positive response. Action taken with epoetin zeta in response to these events was reported as unknown. The outcome for the event of angina pectoris was reported as unknown, and the patient remained hospitalized at the time of the report.

On 12 Mar 2015 (Study Day 830), a day after receiving a dose of epoetin zeta, the patient developed a reported event of apoplexy (ACM) (MedDRA PT: cerebrovascular accident). On the same day, she was hospitalized due to cerebrovascular accident, which also caused persistent/significant disability. It was reported that the patient complained of vision problems. The laboratory results showed normal levels of activated partial thromboplastin time (aPTT) at 27 seconds (normal range [NR]: 23 to 32 seconds), international normalized ratio (INR) at 1.0 (NR not provided), platelet count at $207 \times 10^3/mm^3$ (NR: 150 to $400 \times 10^3/mm^3$), and prothrombin time (PT) at 96% (NR: 70% to 130%). The patient was treated with phenprocoumon and oral systemic anticoagulation therapy. Action taken with epoetin zeta in response to the event was unknown. On 16 Mar 2015 (Study Day 834), the patient's fibrinogen was 481 mg/dL (NR: 210 to 400 mg/dL), while her aPTT, INR, platelet count and PT were within normal limits. On 18 Mar 2015 (Study Day 836), the patient's fibrinogen was 401 mg/dL; and the patient was discharged from the hospital. On an unknown date, the event of cerebrovascular accident was considered resolved with sequelae (persistent/significant disability).

On 23 May 2015 (Study Day 902), the patient died. The cause of the death was not reported.

In the opinion of the Investigator, there was not a reasonable possibility that the events of cerebral ischaemia, cerebrovascular accident, angina pectoris, and death were related to epoetin zeta. The Sponsor concurred with this assessment that there was not a reasonable possibility that the events of cerebral ischaemia, angina pectoris and cerebrovascular accident were related to epoetin zeta. Per Sponsor, the causality for death could not be assessed due to limited information including the cause of death. It was unclear if the death was due to complications of previously reported conditions or to new-onset disease. According to the Sponsor, the patient's multiple cardiovascular risk factors (vascular anomalies, obesity, diabetes, hypertension, and coronary artery disease) outweigh the potential risk from epoetin zeta.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Ge-165-0010

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 3154886, 2016534792

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Embolism (AER# 3154886)	Thromboembolic events
Cerebral infarction (AER# 2016534792)	Subacute cerebral infarction
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	Not applicable

This 79-year-old White male patient was enrolled in post-authorization safety cohort observation study on 22 Jan 2015 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of cerebrovascular disorder, small axial hernia, and vascular nephropathy (all since unknown dates); prostate cancer (diagnosed in 1992); hepatic cyst, diverticulosis, aortectasis, endarterectomy of aorta, sleep apnea syndrome (with continuous positive airway pressure), hypertension, hyperphosphatasemia, lack of vitamin D, generalized atherosclerosis, hypercholesterolemia, secondary hyperparathyroidism, and renal failure (all since 02 May 2007); nephrogenic anemia (since 07 Jul 2010); appendectomy (from 19 May 2011 to May 2011); Mallory Weiss syndrome (from 21 Dec 2015 to January 2016), and nicotine dependence.

The patient began dialysis 7 times per week from 20 Jan 2014 and he started receiving SC epoetin zeta 98 IU/kg/week (3 dosage/week) from 26 Aug 2011. Concomitant medications included clopidogrel, candesartan, metoprolol succinate, lercanidipne hydrochloride, doxazosin mesilate, xipamide, furosemide, calcium carbonate/calcium gluconate/calcium lactate/ergocalciferol, calcium acetate/magnesium carbonate, sodium bicarbonate, colecalciferol, cinacalcet hydrochloride, atorvastatin calcium, and omeprazole.

On an unknown date, the patient experienced a reported event of thromboembolic events (MedDRA preferred term [PT]: embolism). The event of embolism was considered as an important medical event requiring medical or surgical intervention. The details on investigations including examinations, laboratory, diagnostic results, and the treatment given for the event were not reported. The action taken with epoetin zeta in response to the event and the outcome of the event were reported as unknown.

On 30 Sep 2016 (Study Day 618), the patient experienced a reported event of subacute cerebral infarction (MedDRA PT: cerebral infarction) and was hospitalized. It was reported that the patient had no risk factor for thromboembolic events.

On 12 Oct 2016 (Study Day 630), the patient was transferred to another hospital due to sub-acute cerebral infarction for further acute geriatric therapy. The physical findings showed that the patient was awake, oriented, responsive, “acute reduced after stroke”; skin color was normal with moist mucosa, and his defecation and urination were inconspicuous. The patient’s respiratory, cardiac, and abdominal examinations were unremarkable. Extremities were mobile and free of pain, no pain while rapping on spinal area. No relevant edema in lower legs was noted and the patient was in a state after apoplexy and had gait disturbance. The patient was only mobile by rollator. The patient’s vital signs showed blood pressure of 130/70 mmHg, heart rate of 70 beats per minute, with oxygen saturation of 99% under room air. At admission, an electrocardiogram showed normal sinus-rhythm, left axis deviation, and left anterior hemiblock, with no acute signs of disturbance in repolarization. The patient’s troponin T was 0.13 ng/mL (normal range was not provided). Methicillin resistant *Staphylococcus aureus* (MRSA) screening was negative. The neurological condition showed no meningismus. The patient’s pupils were of same size and "middle wide" with normal pupillary light reflex. The patient’s Barthel-index score was 90; Dem Tect was 12 points, GDS (grade of impairment-outcome) score was 1, and Norton-scale score was 29. At admission, risk assessment for fall down (modified in regard to Stratify) was 3 points; timed up and go test was 20 seconds - while walk with rollator and one auxiliary; Clock-test: 1 point, Pain-scaling: left hip: 1/4 -5. The patient underwent intense ergo and physiotherapeutic programs. Physiotherapeutic finding showed the patient was able to realize all transfers by his own. He could walk with rollator, equilibrium (balance) was slightly reduced, and opposition of thumb and little finger on right hand was not possible. Power of left upper extremity had slightly reduced, as well as left lower extremity. Ergo therapeutic findings showed the patient was fully oriented, cognitive very adequate - transfers made by himself. The patient’s general balance was slightly reduced, especially without additive resources. Power of right hand was stronger then left hand. The patient pointed out that fine motor skills of left side were reduced due to the old apoplexy, at admission not noticeable. The hip flexion on left side was also reduced. The power of both lower extremities was reduced, left side more than right side. While performing knee extension left side while sitting a stretching pain was triggered in the respective thigh. The patient’s treatment with ongoing dialysis, his antihypertensives and diuretics dose were adjusted. No action was taken with epoetin zeta in response to the event. On 21 Oct 2016 (Study Day 639), the event of cerebral infarction resolved and the patient was discharged from the hospital. The discharge medications included decreased dose of xipamide, increased dose of furosemide, calcium/vitamin D, calcium acetate/ magnesium carbonate, colecalciferol, cinacalcet, atorvastatin, pantoprazole, and lercanidipine.

On 27 Apr 2017 (Study Day 827), the patient was discontinued from the study as per Investigator decision due to patient’s clinical progress.

The Investigator's causality between the event of embolism and epoetin zeta was not reported. According to the Sponsor, the causality between the event of embolism and the epoetin zeta was not assessable, although epoetin zeta could theoretically increase the risk of

thromboembolic events. The Sponsor stated that a definitive assessment could not be provided without firm timeline, clinical event details and specific event that occurred.

In the opinion of the Investigator, there was not a reasonable possibility that the event of cerebral infarction was related to epoetin zeta or concomitant medications. The Sponsor concurred with this assessment, and reported that there was not a reasonable possibility that the event of cerebral infarction was related to epoetin zeta or concomitant drugs. According to the Sponsor, the patient's elderly age, previous nicotine abuse and underlying conditions of arterial hypertension, hypercholesterolemia, and atherosclerosis were considered significant risk factors for development of cerebral infarction.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Sw-005-0025

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 3023456, 2016461859

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Myocardial infarction (AER# 3023456)	Minor myocardial infarction
Acute myocardial infarction (AER# 2016461859)	NSTEMI
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Causes of Death:	Not applicable

This 53-year-old White male patient was enrolled in post-authorization safety cohort observation study on 13 Sep 2013 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of coronary artery disease with angina, type 2 diabetes mellitus, hyperlipidemia, hypertension, myocardial ischemia, myocardial infarction, drug (Cosmofer) hypersensitivity, vascular graft, hiatus hernia, hypertensive nephropathy, and obesity (all since unknown dates); renal failure (since 20 Jan 2011); and antithrombin III deficiency (0.83 [normal range [NR]: 0.85-1.25], since 29 Jan 2011). The patient was a current smoker. The patient had not been exposed to any other erythropoietin-stimulating agents.

The patient began dialysis 3 times per week from 14 May 2013, and he started receiving SC epoetin zeta at a total dosage of 97 IU/kg/week (1 dosage/week) from 23 May 2013. Concomitant medications included allopurinol, candesartan cilexetil, colecalciferol, alfacalcidol, felodipine, tinzaparin sodium, calcium carbonate, metoprolol tartrate, cinacalcet hydrochloride, ascorbic acid/nicotinamide/pyridoxine hydrochloride/riboflavin/thiamine hydrochloride, acetylsalicylic acid, saccharated iron oxide, furosemide, glyceryl trinitrate, simvastatin isosorbide mononitrate, atorvastatin, paracetamol, lanthanum carbonate, omeprazole, oxycodone hydrochloride, and hydroxyzine.

On 04 Sep 2015 (Study Day 722), two days after receiving a dose of epoetin zeta, the patient experienced persistent chest pain which did not improve with nitroglycerin. On 06 Sep 2015 (Study Day 724), the patient was taken to the emergency department and was diagnosed with a reported event of minor myocardial infarction (MedDRA preferred term [PT]: myocardial infarction) manifested as angina pectoris (with an onset date of 04 Sep 2015), which was a life-threatening event resulting in hospitalization. The investigations performed on an unspecified date showed troponin T ranging from 47 to 57.97 mg/L (normal range was not

provided) and a myocardial scintigraphy showed a presence of possible small myocardial injury, and an electrocardiogram (ECG) showed no new changes. The patient was treated with morphine. No action was taken with epoetin zeta in response to the event. On 08 Sep 2015 (Study Day 726), the patient was asymptomatic; and the event of myocardial infarction was considered resolving and the patient was discharged from the hospital on an unknown date.

On 10 Nov 2015 (Study Day 789), a coronary angiography showed spread changes in native coronary vessels: occluded left anterior descending (LAD) artery and several stenoses in the circumflex artery (as previously noted); occluded the right coronary artery; and left internal mammary artery was open but LAD distal of the anastomosis was occluded, unchanged venous graft to D1, M1, and M2 had an ostial non-significant stenosis and degenerative alterations distally but no stenoses; and venous graft to posterior descendens was generally narrow but had no definable stenoses.

On 04 Apr 2016 (Study Day 935), four days after receiving a dose of epoetin zeta, the patient was diagnosed with a reported event of NSTEMI (MedDRA PT: acute myocardial infarction) and was hospitalized. On the same day, an ECG showed sinus rhythm, a chamber frequency of 78 s/m, PQ time of 204 msec, QRS duration of 100 msec, QT/QTc of 448/510 msec, and PR-T-axis of 60-4 144. The ECG indicated abnormal repolarization, suspected pathologically delayed atrioventricular conduction, scattered leads with prolonged QT time, and anteroseptal infarction and ischemia. The patient's troponin T values at 3 different time intervals showed 63 ng/L, 170 ng/L, and 969 ng/L (NR: <15 ng/L). His creatinine was at alarming limit of 997 µmol/L (NR: 60 to 105 µmol/L) and platelet count was decreased at 123×10^9/L (NR: 140 to 350×10^9/L). No action was taken with the epoetin zeta in response to the event. On 07 Apr 2016 (Study Day 938), the patient's laboratory investigation showed creatinine of 1011 µmol/L, potassium of 4.6 mmol/L (NR: 3.5 to 4.4 mmol/L), C-reactive protein of 26 mg/L (NR: <10 mg/L), and platelet count of 133×10^9/L. On the same day, the patient was discharged from the hospital. The treatment provided for the event was unknown. On 13 May 2016 (Study Day 974), the event of acute myocardial infarction resolved.

On 14 Sep 2016 (Study Day 1098), the patient completed the study.

In the opinion of the Investigator, there was a reasonable possibility that the event of myocardial infarction was unlikely related to epoetin zeta. The Sponsor did not concur with this assessment and stated that the event of myocardial infarction was possibly related to epoetin zeta based on medical plausibility. Per Sponsor, though multiple risk factors were noted in the patient, epoetin zeta still be considered to contribute in the development of thromboembolic events.

In the opinion of the Investigator, there was not a reasonable possibility that the event of acute myocardial infarction was related to epoetin zeta. The Sponsor concurred with this assessment that the reported event of acute myocardial infarction was not related to epoetin zeta. According to the Sponsor, the patient's underlying diseases of ischemic heart disease, diabetes mellitus, hyperlipidemia, and hypertension and multiple risk factors for thromboembolitic events including obesity, smoking, antithrombin III deficiency provided

the likely explanation to the development of event. The Sponsor did not consider the event as related to any concomitant medication or clinical trial procedure.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SERIOUS ADVERSE EVENTS OF SPECIAL INTEREST NARRATIVE

Patient ID Number: Sw-005-0040

Study Treatment: Epoetin zeta

Serious Adverse Event Reference (AER) Case Numbers: 3214713, 2017001948

The following narrative criterion was met:

- Serious Adverse Event (SAE) of Special Interest

MedDRA Preferred Term:	**Investigator Reported Term:**
SAEs of Special Interest:	
Acute myocardial infarction (AER# 3214713)	NSTEMI
Transient ischaemic attack (AER# 3214713)	Transient cerebral ischemic attack
Pulmonary embolism (AER# 2017001948)	Prob. pulmonary embolism
Drug Permanently Discontinued Due to the SAEs of Special Interest?	No
Cause of Death:	Not applicable

This 67-year-old White male patient was enrolled in post-authorization safety cohort observation study on 29 Aug 2014 (Study Day 1) and received subcutaneous (SC) epoetin zeta for the treatment of renal anemia.

The patient had a medical history of glomerulonephritis, hyperlipidemia, myocardial ischemia, coronary artery disease, aortic dilatation, obesity (body mass index of 33.3 kg/m^2), and myocardial infarction (all since unknown dates); renal failure (since 02 Jan 1978); hypertension (since 1980); type 2 diabetes mellitus (since 2000); adenocarcinoma operation (2007); rectal cancer (since 2007); cerebrovascular accident (2009); pulmonary metastasis and lobectomy (both in April 2013). The patient was a current smoker and had a family history of cerebrovascular disorder.

The patient began dialysis 3 times per week from 22 Jul 2014 and he started receiving SC epoetin zeta 39 IU/kg/week (1 dosage/week) from 22 Jul 2014. Concomitant medications included acetylcysteine, doxazosin mesilate, atorvastatin calcium, cyanocobalamin, iron dextran, colecalciferol, lidocaine/prilocaine, enalapril maleate, felodipine, folic acid, lanthanum carbonate, furosemide, tinzaparin sodium, insulin human/insulin human injection/isophane, calcium carbonate, loperamide hydrochloride, macrogol/potassium chloride/sodium bicarbonate/sodium chloride, sodium bicarbonate, ascorbic acid/nicotinamide/pyridoxine hydrochloride/riboflavin/thiamine hydrochloride, oxycodone hydrochloride, paracetamol, pantoprazole sodium sesquihydrate, sodium polystyrene sulfonate, amoxicillin trihydrate/clavulanate potassium, acetylsalicylic acid, clopidogrel, erythrocytes, alfacalcidol, calcium globionate, dimeticone/loperamide hydrochloride, ezetamibe, codeine phosphate/paracetamol, oxazepam, zolpidem tartrate, ticagrelor, and sevelamer.

On 14 Nov 2015 (Study Day 443), 5 days after receiving a dose of epoetin zeta the patient developed a reported event of NSTEMI (MedDRA preferred term [PT]: acute myocardial infarction), which was a life-threatening event leading to hospitalization on the same day. On the same day, the patient's laboratory investigations showed C-reactive protein (CRP) of 19 mg/L (normal range [NR]: <10 mg/L), platelet count of 382 × 10^9/L (NR: 140 to 350 × 10^9/L), and troponin T of 96 ng/L (NR: <15 ng/L). On 15 Nov 2015 (Study Day 444), the patient's troponin T was 133 ng/L and 225 ng/L. On 17 Nov 2015 (Study Day 446), the patient underwent a coronary angiography via right radial artery which showed significant stenosis in the middle section of left anterior descending (LAD) artery with atheromatosis in the rest of the vessel; atheromatosis without significant stenoses in the circumflex artery (collateral circulation to right vessel) and right coronary artery ectasia with significant stenosis in proximal and middle sections. On 18 Nov 2015 (Study Day 447), the patient's laboratory investigations showed activated partial thromboplastin time of 25 seconds (NR: 24 to 32 seconds), blood calcium level of 2.23 mmol/L (NR: 2.15 to 2.50 mmol/L), phosphorus of 2.4 pg (NR: 0.75 to 1.4 pg), potassium of 5.1 pg (NR: 3.4 to 4.4 pg), sodium of 137 mmol/L (NR: 137 to 145 mmol/L), and international normalized ration of 1.0 (NR: 0.8 to 1.2), platelet count of 337 × 10^9/L, and white blood cell (WBC) count of 9.1 × 10^9/L (NR: 3.5 to 8.8 × 10^9/L). On 04 Dec 2015 (Study Day 463), a computerized tomography (CT) of head showed no intracranial bleeding, no evidence of recent infarction, normal width, non-dislocated cerebrospinal fluid spaces and no radiological evidence of increased intracranial pressure or intracranial expansive processes.

On 23 Dec 2015 (Study Day 482), the patient underwent a transesophageal echocardiography which showed the whole unchanged results compared with earlier examinations, the most recently performed on 15 Dec 2015 (Study Day 474), with a slightly changed aortic valve and hyperechoic in the mitral valve ring with a number of irregularities, probably made up of ring calcification. The right-sided valves were gracile and without change. No suspected endocarditis changes in the heart chambers. It was reported that the patient had double vessel coronary artery disease. On 28 Dec 2015 (Study Day 487), a percutaneous coronary intervention on LAD was carried out. The right coronary artery was left for clinical evaluation. On 28 Dec 2015 (Study Day 487), the laboratory result showed WBC count of 10.0 × 10^9/L, platelet count of 354 × 10^9/L, CRP of 36 mg/L, sodium at 138 mmol/L, and potassium of 4.4 mmol/L. No action was taken with epoetin zeta in response to the event of acute myocardial infarction. On 30 Dec 2015 (Study Day 489), the event resolved and the patient was discharged from the hospital.

On 27 Jan 2016 (Study Day 517), the patient fell out of bed hitting his right shoulder to the edge of the bed, with a potential short episode of loss of consciousness. The patient could not recall the event. The patient remembered that the shoulder area was hurt immediately when he woke up on the floor. The tenderness in his shoulder remained for about 24 hours. The patient had no bruising developed and did not hit his head during the fall, and he was completely functional afterwards.

On the next day (Study Day 518) morning, the patient began experiencing disturbed motor movements in the right hand, and partly a band-shaped loss of sensation corresponding to dermatome C3-C5 on right. The patient reported that he still had pain in right shoulder, and later, he was suddenly unable to hold the dishwashing brush in his right hand. The patient

experienced mainly a weakness in his grip and more precisely in the flexion of fingers (second to fifth digits). His thumb was unaffected, and he could move his arm and wrist and extend the fingers in his right hand. However, he experienced the motor movement disturbances; he also started to be affected by a sudden loss of sensation corresponding to a just over 5 cm wide band including the lateral right upper arm, right shoulder, shoulder blade and up towards the top part of the neck (i.e. corresponding to dermatome C3-C5). No associated paresthesia was reported. The loss of sensation disappeared after around one hour. The patient was taken to the emergency room (ER) and his motor movement disturbance remained significantly longer and subsided while he was in the ER. On the same day (Study Day 518), the patient was diagnosed with a reported event of transient cerebral ischemic attack (MedDRA PT: transient ischaemic attack, with an onset date of 27 Jan 2016) and was admitted for telemetry, investigations, and carotid duplex. Head CT showed no new infarction or bleeding. Carotid duplex scan showed the formation of plaque with normal flow rate, without any significant stenosis. The telemetry was unremarkable. The laboratory results showed raised troponin without dynamics and raised N-terminal prohormone brain natriuretic peptide, most likely related to heart failure and secondary to ischemic heart disease. The patient was treated with Behepan and Folacin due to the elevated levels of homocysteine, and pantoprazole. The patient continued treatment with acetylsalicylic acid and clopidogrel. The patient quickly came back to his habitual condition and was functioning well. No action was taken with epoetin zeta in response to the event. On the same day (Study Day 518), the event of transient ischaemic attack resolved. On 29 Jan 2016 (Study Day 519), an extensive Carotid duplex scan showed bilateral moderate formation of plaque. However, regular flow speeds in all assessed vessels with no significant stenosis. The patient was discharged from the hospital on an unknown date.

On 06 Dec 2016 (Study Day 831), the patient underwent arteriovenous fistula revision.

On 22 Dec 2016 (Study Day 847), the patient developed dyspnea when speaking, despite oxygen, and was hospitalized. He had breathing related pain but no chest pain on exercise, fever or cough. On the same day, the laboratory investigations showed arterial blood gases: pH of 7.47 (NR: 7.36 to 7.45), pO2 of 8.4 kPa (NR: 10 to 13.5 kPa), base excess of 4 mmol/L (NR:-3 to 3 mmol/L), bicarbonate of 27.9 mmol/L (NR: 19 to 26 mmol/L), and oxygen saturation of 93% (NR: ≥95%). The patient's CRP was 27 mg/L (NR: <10 mg/L), and blood pressure was 179/89 mmHg with an oxygen saturation ranging between 84% and 86% (NR: 90% to 100%). An electrocardiogram (ECG) showed a regular rhythm at 74 beats per minute, left-sided branch block, with no change concordance compared to previous ECG. The pulmonary auscultation revealed no breath sounds on right, basal crepitation on left side with no audible wet rales. It was difficult to determine the attenuation of percussion tone on the left side, with no clear attenuation. No wheezing was noted. A diagnostic CT for pulmonary embolism showed status post right-sided pulmonary surgery; there was one contrast cutout in right under lobe artery in connection to a pair of clips from the pulmonary surgery. The results showed suspected pulmonary embolus; however, tumor ingrowth into the vessel could not be completely ruled out. No additional pulmonary changes were noted. There was pleural fluid of approximately 5 mm thick stratification on the left lung and a minimal amount of pleural fluid was also on the right lung. Septal thickening was suspicious for some decompensation. Multiple mediastinal lymph nodes were individually increased by a few millimeters in size since 09 Nov 2016. On 22 Dec 2016 (Study Day 847), the patient

was diagnosed with a reported event of probable pulmonary embolism (MedDRA PT: pulmonary embolism), which was a life-threatening event resulting in hospitalization. On 23 Dec 2016 (Study Day 848), the patient's CRP was 29 mg/L and N-terminal prohormone brain natriuretic peptide was >35000 ng/L (NR: <900 ng/L). On 24 Dec 2016 (Study Day 849), a CT thorax with intravenous contrast showed no new changes since the last CT on 22 Dec 2016. The patient was treated with ipratropium, salbutamol, tinzaparin, clopidogrel, and oxazepam. No action was taken with epoetin zeta in response to the event. On 05 Jan 2017 (Study Day 861), the patient was discharged from the hospital and the event of pulmonary embolism was considered resolving.

On 28 Aug 2017 (Study Day 1096), the patient completed the study.

In the opinion of the Investigator, there was not a reasonable possibility that the events of acute myocardial infarction and transient ischaemic attack were related to epoetin zeta. According to the Investigator, the event of transient ischaemic attack was due to known stenosis of LAD and RCA, and cerebrovascular disorder. The Sponsor concurred with this assessment, and reported that there was not a reasonable possibility that the events of acute myocardial infarction and transient ischaemic attack were related to epoetin zeta. According to the Sponsor, the patient had numerous cardiac comorbidities and risk factors which outweigh potential risk from epoetin zeta.

In the opinion of the Investigator, there was not a reasonable possibility that the event of pulmonary embolism was related to epoetin zeta, concomitant medications, or a clinical trial procedure. According to the Investigator, the recent surgery of revision of AV fistula and positive family history of cerebrovascular disease were risk factors for thromboembolic events. The Sponsor did not concur with this assessment, and reported that there was a reasonable possibility that the event of pulmonary embolism was possibly related to epoetin zeta. Per Sponsor, the patient's underlying rectal cancer and pulmonary metastasis might provide an alternative explanation.

This narrative reflects data from the safety database as of 23 Jul 2020 and the clinical database as of 12 Aug 2020.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	24	JAN	1962	49 Years	Female	46.00 kg	13	DEC	2011	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously, for the treatment of renal anaemia. This report describes case of myocardial infarction.
This case describes a 49-year-old female patient who received treatment with Retacrit (epoetin zeta, 5000 UI, subcutaneous, 3/week; batch number not reported) for renal anaemia from 10-Mar-2011 until 16-Dec-2011.
Medical history

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 5000 IU, Freq: 1 Week, Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 09-JUL-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPINE (AMLODIPINE) ; 10-OCT-2011 / 30-DEC-2011
#2) CALCITRIOL (CALCITRIOL) ; 10-FEB-2011 / 30-DEC-2011
#3) ENOXAPARIN (ENOXAPARIN) ; 13-NOV-2010 / 30-DEC-2011
#4) EPARGRISEOVIT (ASCORBIC ACID, CYANOCOBALAMIN, FOLIC
#5) EUTIROX (LEVOTHYROXINE SODIUM) ; 07-OCT-2010 / 30-DEC-2011
#6) FULCROSUPRA (FENOFIBRATE) ; 20-MAY-2011 / 30-DEC-2011

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1206113

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

included hypertension and thrombosis on 22-Jun-2000. Risk factor was thrombosis deep vessel lower extremities on 17-Dec-2010. The patient previously received Neorecormon (epoetin beta; 6,000 UI/week, route of administration not reported) from 23-Jun-1997 until 29-Jul-1997 and Eritrogen (epoetin alfa; 3000 UI/week, route of administration not reported) from 30-Jul-1997 until 09-Mar-2011 with Hb of 8.5 g/dl (normal range:12-16). Concomitant medications included Calcisex (calcitriol, 3 vials/week,) for prophylaxis from 10-Feb-2011 until 30-Dec-2011, Epargriseovit (folic acid, Vit. B12, Vit B3, and Vit. C; 3 vials/week) for prophylaxis from 07-May-2011 to present, Fulcrosupra (fenofibrate, 1 cap/day) for dislipedemia from 20-May-2011 until 30-Dec-2011, Pariet (rabeprazole, 40 mg/day) for gastrointestinal prophylaxis from 28-Dec-2008 until 30-Dec-2011, Eutirox (levothyroxine, 111 mcg/day) from 07-Oct-2011 until 30-Dec-2011 for hypothyroidism, Amlopidina (amlodipine, 25 mg/day) for hypertension from 10-Oct-2011 until 30-Dec-2011 and Enoxaparina (enoxaparin, 8000UI/day) for prophylaxis from 13-Nov-2010 until 30-Dec-2011; routes of administration not reported.
On an unknown date, the patient began hemodialysis. On 10-Mar-2011, the patient began treatment with epoetin zeta. On 09-Jul-2011, dose of epoetin zeta was changed to a dose of 5000 UI/week with Hb of 13.3 g/dl and 13.6 g/dl, before and after the dose waschanged. On 28-Sep-2011, the patient's hemoglobin was 11.3 g/dl. On 12-Nov-2011, dose of epoetin zeta was changed to 6000 UI/week with Hb of 10.4 g/dl and 9.9 g/dl, before and after the dose was changed. On 29-Nov-2011, dose was changed to 9000 UI/week with Hb of 9.9 g/dl and 10.2 g/dl before and after the dose was changed. It was also reported that last dose of epoetin zeta administered was on 16-Dec-2011. On 13-Dec-2011, the patient experienced myocardial infarction. On 14-Dec-2011, investigations revealed integral PTH 126 PG/ML (normal range: 12-65), ferritin 1104 ng/ml (normal range:13-150), BUN 167 mg/dl (normal range:10-50), glycemia 74 mg/dl (normal range:70-110), blood uric acid 6.5 mg /dl (normal range:2.4-5.7), total bilirubin 0.3 mg /dl (normal:<1.0), blood creatinine 9.95 mg/dl (normal range:0.50 -0.90), total cholesterol 163 mg/dl (normal range not reported), tryglyceridemia 145 mg/dl (normal range:<200), blood sodium 136 mEq/l (normal range:133-145), blood potassium 5.3 mEq/l (normal range:3.3-5.1), serum calcium 9.7 mg/dl (normal range:8.6-10.2),serum phosphorous 5.7 mg/dl (normal range: 2.7-4.5), alkaline phosphatase 35 U/l (normal range: 35-104), AST 23 U/l (normal:<32), ALT 13 U/l (normal: <31), gamma GT 13 U/l (normal range: 6-42), blood iron 80 mcg/dl (normal range: 37-145), transferrinemia 265 mg/dl (normal range: 200-360), platelets 134 migl/mmc (normal range: 150-450), blood leucocytes 6.4 migl/mmc (normal range: 4-10), blood erythrocytes 4.63 mil/mmc (normal range: 4.2-5.4), hemoglobin 10.2 g/dl (normal range: 12-16), hematocrit 33.4 % (normal range: 36-46), mean corpuscular volume 72.1 femolitri (normal range: 77-91), mean hemoglobin value 22.1 pg (normal range: 26-32), mean hemoglobin concentration 30.6 g/dl (normal range: 32-36), index of distribution of erythrocytes volume 20.2 % (normal range: 13.8-15.0) and PCR (protein C reactive) 0.2 mg/dl (normal:<0.5). She was hospitalised from 22-Dec-2011 until 30-Dec-2011. Treatment included trinitroglyceride (10 mg/day), clopidogrel (75 mg/day), and ASA (100 mg/day); routes of administration not reported. On 21-Dec-2011, patient recovered from myocardial infarction. The reporter's causality assessment between myocardial infarction and epoetin zeta was not related.
Received English translation of Italian narrative on 02-Mar-2012. Follow-up report created to reflect additional information regarding adverse event details and laboratory/diagnostic tests. On 20-Dec-2011, the patient visited a cardiologist because of prolonged retrosternal pain for about two hours during dialysis on 19-Dec-2011. During the visit, the patient was asymptomatic for angina. The patient reported that the onset of symptoms was last week (date unspecified) with first episode that persisted only for a few minutes. The only prolonged episode was 19-Dec-2011 with retrospinal pain radiating to the jugular, shoulders and arms, and associated with mild dyspnea. Intensity was reported as moderate. General and physical examination showed heart sounds, rhythmic, valid, systolic murmur 1/6 at the tip. Vesicular murmur, bronchial noises in the center field and right pulmonary apex that vary with the coughing. Echocardiograph compared to the previous exam showed left ventricle of normal volume, mild concentric hypertrophy, appearance of basal septum hypokinesia and akinesia of basal inferior wall, left atrium and right sections normal, transmitral pattern remain from impaired ventricular relaxation, mitral leaflet thickened with minimal mitral regurgitation, sclerosis of the aortic cusps associated with mild to moderate valvular insufficiency, minimum tricuspid regurgitation from which it was estimated that pressure of the small circle was within normal limits (estimated PAP 29 mmHg), and Inferior vena cava normal (18/5mm). Myocardial enzymes showed positive: TnL 0.74 microg/L and CK-MB 13.42 ng/ml (normal ranges not reported). ECG showed RS with the appearance of altered repolarization in lower dd. BP (blood pressure) was 110/75 mmHg. The patient was applied with nitro patch 10 mg. The cardiologist conclusion was acute coronary syndrome and appearance of abnormalities in segmental kinetics of left ventricular and positive myocardial enzymes. The patient was referred for admission and continuation of treatment. 12-Mar-2012: Follow up report created for data entry correction for information previously received on 23-Feb-2012. Changes will be made on the dosage unit of suspect drug which has been left blank in the previous reports. 23-Jan-2014: Data entry correction was made regarding laboratory data, suspect drug, and concomitant medications. Height and weight were deleted and laboratory results of general/special examination and echocardiography were reflected in the laboratory section. In the narrative, active substance names of Epargriseovit, Fulcrosupra, Pariet, and Eutirox should not be included as the information was not provided by the reporter while therapy start date of Eutirox should be 07-Oct-2010. Frequencies of Fulcrosupra, Pariet, Eutirox, amlodipine, and enoxaparin were populated.
Therapy start date of amlodipine was corrected to 10-Oct-2010 in the concomitant drug section. Therapy end date of epoetin zeta was deleted in the suspect drug section. Action taken with the suspect drug in response to the adverse event was not reported.

Amendment: This follow-up report is being submitted to amend previously reported information: remove previously mentioned "prior to the event" in narrative.

Case Comment: Overall case causality: Not related Consider events to be due to natural pathogenesis of atherosclerosis and

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

myocardial infarction given the patient's multiple risk factors. Overall case causality (Follow-up 09 Mar 2012): Not related No change in assessment Overall case causality (Follow-up 13 Mar 2012): Not related No change in assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	14-DEC-2011	Alanine aminotransferase	13 IU/l	
2	14-DEC-2011	Aspartate aminotransferase	23 IU/l	
3	14-DEC-2011	Blood alkaline phosphatase	35 IU/l	104 3.5
4	14-DEC-2011	Blood bilirubin	0.3 mg/dl	
5	14-DEC-2011	Blood calcium	9.7 mg/dl	10.2 8.6
6	14-DEC-2011	Blood cholesterol	163 mg/dl	
7	20-DEC-2011	Blood creatine phosphokinase MB	13.42, NG/L	
8	14-DEC-2011	Blood creatinine	9.95 mg/dl	0.90 0.50
9	14-DEC-2011	Blood glucose	74 mg/dl	110 70
10	14-DEC-2011	Blood iron	80, MCG/DL	145 37
11	14-DEC-2011	Blood parathyroid hormone	126, PG/ML	65 12
12	14-DEC-2011	Blood phosphorus	5.7 mg/dl	4.5 2.7
13	14-DEC-2011	Blood potassium	5.3 mEq/l	5.1 3.3
14	20-DEC-2011	Blood pressure measurement	110/75 mmHg	
15	14-DEC-2011	Blood sodium	136 mEq/l	145 133
16	14-DEC-2011	Blood test	20.2 %	15.0 13.8
17	14-DEC-2011	Blood triglycerides	145 mg/dl	
18	14-DEC-2011	Blood urea	167 mg/dl	50 10
19	14-DEC-2011	Blood uric acid	6.5 mg/dl	5.7 2.4
20		Body mass index	22.18, Unknown	
21	14-DEC-2011	C-reactive protein	0.2 mg/dl	
22	20-DEC-2011	Echocardiogram Pressure of the small circle within normal limits, Unknown	Pressure of the small circle within normal limits,	
23	20-DEC-2011	Echocardiogram	Estimated PAP 29 mmHg	
24	20-DEC-2011	Echocardiogram	Transmitral pattern	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			remain, Unknown	
25	20-DEC-2011	Echocardiogram	Sclerosis of the aortic cusps, Unknown	
26	20-DEC-2011	Echocardiogram	Mitral leaflet thickened, Unknown	
27	20-DEC-2011	Echocardiogram	Minimum tricuspid regurgitation, Unknown	
28	20-DEC-2011	Echocardiogram	Minimal mitral regurgitation, Unknown	
29	20-DEC-2011	Echocardiogram	Mild concentric hypertrophy, Unknown	
30	20-DEC-2011	Echocardiogram	Left ventricle of normal volume, Unknown	
31	20-DEC-2011	Echocardiogram	Inferior vena cava normal (18/5mm), Unknown	
32	20-DEC-2011	Echocardiogram	Impaired ventricular relaxation, Unknown	
33	20-DEC-2011	Echocardiogram	Appearance of basal septum hypokinesia, Unknown	
34	20-DEC-2011	Echocardiogram	Akinesia of basal inferior wall, Unknown	
35	20-DEC-2011	Echocardiogram	Left atrium and right sections normal, Unknown	
36	20-DEC-2011	Echocardiogram	Mild to moderate valvular insufficiency, Unknown	
37	14-DEC-2011	Gamma-glutamyltransferase	13 IU/l	42 6
38	14-DEC-2011	Haematocrit	33.4 %	46 36
39		Haemoglobin	10.4 g/dl	16 12
40		Haemoglobin	13.6 g/dl	16 12
41		Haemoglobin	9.9 g/dl	16 12
42		Haemoglobin	10.2 g/dl	16 12
43		Haemoglobin	13.3 g/dl	16 12
44	28-SEP-2011	Haemoglobin	11.3 g/dl	16 12
45	14-DEC-2011	Haemoglobin	10.2 g/dl	16 12
46	14-DEC-2011	Mean cell haemoglobin	22.1 pg	32 26
47	14-DEC-2011	Mean cell haemoglobin concentration	30.6 g/dl	36 32
48	14-DEC-2011	Mean cell volume	72.1 femtolitri, Unknown	91 77
49	20-DEC-2011	Myocardial necrosis marker	positive: 0.74, MCG/L	

Mfr. Control Number: 1206113

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
50	20-DEC-2011	Physical examination	Bronchial noises in center field, Unknown	
51	20-DEC-2011	Physical examination Systolic murmur 1/6 at the tip,veiscular murmur, Unknown	Systolic murmur 1/6 at the tip,veiscular murmur	
52	20-DEC-2011	Physical examination General/special examination (20-Dec-2011): Right pulmonary apex that vary with each coughing, Unknown	Right pulmonary apex that vary with each coughing,	
53	20-DEC-2011	Physical examination	Heart sounds, rhythmic, valid, Unknown	
54	14-DEC-2011	Platelet count	134 migl/mmc, Unknown	450 150
55	14-DEC-2011	Red blood cell count	4.63 mil/mmc, Unknown	5.4 4.2
56	14-DEC-2011	Serum ferritin	1104 ng/ml	150 13
57	14-DEC-2011	Transferrin	265 mg/dl	360 200
58	14-DEC-2011	White blood cell count	6.4migl/mmc, Unknown	10 4

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	5000 IU, Freq: 1 Week, Interval: 3; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	10-MAR-2011 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	6000 IU, Freq: 1 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	12-NOV-2011 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #4	6900 IU, Freq: 1 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	29-NOV-2011 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) EPARGRISEOVIT (ASCORBIC ACID, CYANOCOBALAMIN, FOLIC ACID, NICOTINAMIDE) ; 07-MAY-2011 / Unknown

#7) PARIET (RABEPRAZOLE SODIUM) ; 28-DEC-2001 / 30-DEC-2011

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. The patient previously received Neorecormon (epoetin beta; 6,000 UI/week, route of administration not reported) from 23-Jun-1997 until 29-Jul-1997 and Eritrogen (epoetin alfa; 3000 UI/week, route of administration not reported) from 30-Jul-1997 until 09-Mar-2011 with Hb of 8.5 g/dl (normal range:12-16).

Mfr. Control Number: 1206113

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History 22-Jun-2000; stop date UNK	Thrombosis (Thrombosis);
Unknown	Relevant Med History Risk Factor: 17-Dec-2010	Deep vein thrombosis (Deep vein thrombosis);
30-JUN-1997 to 09-MAR-2011	Past Drug Event	ERITROGEN (ERITROGEN /00909301/); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
23-JUN-1997 to 29-JUL-1997	Past Drug Event	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	GERMANY	09	DEC	1947	64 Years	Female	64.00 kg	03	FEB	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplex [Cerebrovascular accident]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia. This report describes case of apoplex. This
case describes a 64-year-old female patient who received treatment with Retacrit 6000 IU/0.6 ml (epoetin zeta, subcutaneous, 1/week; batch number not reported) for renal anaemia from 23-Feb-2011. Medical history included smoking,

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 6000 IU, Freq: 1 Week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 23-FEB-2011 / 30-JAN-2012	#1) 342 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACTRAPID /00646001/ (INSULIN HUMAN) ; Unknown
#2) ALLOPURINOL ALPHARMA (ALLOPURINOL) ; Unknown
#3) CALCITRIOL (CALCITRIOL) ; Unknown
#4) DECORTIN H (PREDNISOLONE) ; Unknown
#5) DEKRISTOL (COLECALCIFEROL) ; Unknown
#6) DREISACARB (CALCIUM CARBONATE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1232463

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-MAR-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

chronic nicotine abuse,chronic alcohol abuse to Jan 2008, hyperlipidemia, ischemic heart disease since 1999, arterial hypertension, intermittent atrial fibrillation from Feb 2012, apoplexia on Sep 2011 and Feb2012, infarction of the right brain in 2012, chronic kidney failure stage III-IV, benign nephrosclerosis, diabetic nephropathy DDG-stage 2b (formal, no retinopathy), secondary renal hyperparathyroidism, Vitamin D deficiency, renal anaemia, metabolic acidosis, diabetes mellitus Type 2, out of control Feb 2009:changed to insulin, status post endarterectomy right Sep 2011, ischemic stroke right Sept 2011, Feb 2012 Re-stroke, cerebral seizure Feb 2012, coronary heart disease, history status post anterior myocardial infarction 1999, hypothyroidism, status post thyroidectomy for benign nodes, adrenal hypofunction in 2000, status post septic osteonecrosis both sides Nov 08, TEP right (left May 09), portal hypertension, history status post portal vein thrombosis, chronic calcifying pancreatitis, depression, anxiety, reflux oesophagitis I (Gastro April 08), status post cholecystectomy 1968 for symptomatic cholecystolithiasis (+ bile duct revision), acute renal failure in 2000 in sepsis, rhabdomyolysis, long term ventilation, PEG tube feeding, and chronic constipation under phosphate therapy. Concomitant medications included L-thyroxin 150 Henning Tabl. (thyroxine, 1-0-0-0), Torasemid AL 20 mg Tabl. (torasemide, 1-1/2-0-0), allopurinol AL 300 Tabl. (allopurinol, 0-0-1/2-0), Mirtazapin Biomo 30 mg Filmtabl. (mirtazapine, 0-0-1-0), Dreisacarb Filmtabl. (calcium carbonate, 1-2-1-0; in-between meals, 1 additional), Dekristol 20000 I.E. cap (colecalciferol, 1-0-0-0 every 14 days), Calcitriol Gry 0.25 ug cap (calcitriol, 1-0-0-0), Zopiclon Teva 7.5 mg Filmtabl. (zopiclone, 0-0-0-1/2 if necessary), Lantus 100 E/ml Patrone Zylinderamp (insulin glargine, 0-0-10-0), Actrapid Penfill 100 I.E/ml Zylinderamp. (insulin, according to the 50 mg rule), Novalgin 500 mg Filmtabl. (novaminsulfone, 2-2-2-0) for pains only, Keppra 500 mg Filmtabl. (levetiracetam al, 1-0-1-0), Sertralin AbZ 100 mg Filmtabl. (sertraline, 1-0-0-0), Ranitic 300 Filmtabl. (ranitidine, 1/2-0-0-0), simvastatin AbZ 20 mg Filmtabl. (simvastatin, 0-0-1-0), Decortin H 10 mg Tabl. (prednisolone, 1/2-0-0-0), Leflunomid Ratiopharm 10 mg coated tabl (leflunomide, 1-0-0-0) and Ferrlecit 62.5 mg Amp. (sodium ferric gluconate, as a short infusion each time blood samples were taken); doses and routes of administration not reported, all for unknown indications. From 23-Feb-2011, the patient received epoetin zeta. On 03-Feb-2012, the patient experienced apoplexy. The patient was admitted as an in-patient due to a tonic-clonic seizure. Neurological findings showed that the patient was somnolent after diazepam injection, easily roused and could follow instructions. The patient's cranial nerve status was normal, with no tongue bite. The patient had low grade residual left hemiparesis and no sensitive deficit. MER with emphasis on left, Babinski positive on the left. The patient was vegetatively normal. Standing and walking were not checked during admission. Clinical neurological tests found a residual hemiparesis on the left after infarction of the right brain in 2010. In the initial cerebral CT, an older ischemic lesion was found on the right side of the brain. The subsequent MRI of the brain, however showed a fresh ischemia in the area of the old infarct. Given the history, clinical symptoms, vascular diagnosis and imgaing the cerebral ischemia, which had occurred with intermittent atrial fibrillation according to TOAST criteria, was due to a cardiac-embolic event. Investigation on 03-Feb-2012 revealed leukocytes 13.02 Tsd/ul (normal range: 4.40-11.30), haemoglobin 12.5 g/dl (12.3-15.3), thrombocytes 264 x 10**9/l (180-370), erythrocytes 4.86 Mill/ul (4.10-5.10), MCV 82 fl (80-96), MCH 25.7 pg (27-33), MCHC 31.3 g/dl (32-36), haematocrit 40.0 % (35.0-45.0), quick 38 % (70-120), INR 2.12 (0.90-1.40; units not reported), and PTT 47 sec (20-40). 11/sec-alphaEEG showed right temporal lesion and no signs of increased cerebral seizure readiness. On 06-Feb-2012, investigations revealed leukocytes 5.48 Tsd/ul (4.40-11.30), haemoglobin 10.0 g/dl (12.3-15.3), thrombocytes 153 x 10**9/l (180-370), erythrocytes 3.88 Mill/ul (4.10-5.10), MCV 81 fl (80-96), MCH 25.6 pg (27-33), MCHC 31.6 g/dl (32-36), haematocrit 31.5 % (35.0-45.0), neutrophil absolute 3.33 Tsd/ul (2.00-6.30), lymphocyte absolute 1.39 Tsd/ul (1.00-3.60), monocyte absolute 0.50 Tsd/ul (0.08-0.54), eosinophil absolute 0.16 Tsd/ul (0.08-0.36), basophil absolute 0.03 Tsd/ul (0.01-0.09), segmenters 60 % (normal range not reported), and banded/stab cells 2 % (normal range not reported). On 07-Feb-2012 PTT showed 44 sec (20-40), 52 sec on 08-Feb-2012 and 45 sec on 09-Feb-2012. On 13-Feb-2012 Quick test showed 26 % (70-120), INR 3.04 (0.90-1.40, units not reported). On 14-Feb-2012, duplex sonography of the extracranial carotid arteries showed signs of the angiosclerosis in the carotid area but was otherwise normal. Temporal sounding on both sides via Transcranial duplex sonography showed no bone windows. On 16-Feb-2012, Quick test showed 32 % (70-120), INR 2.52 (0.90-1.40, units not reported). On an unknown date, radiologic diagnosis (oral findings) were as follows: CCT: old ischemia on the right side of the brain; no fresh ischemia and no bleeding. MRT of skull: old lesion with new infarcted area on the right side. Chest x-ray results were not reported. Cardiologic diagnosis: ECG showed sinus rhythm normal. 24-hr ECG showed full sinus rhythm with HF between 54-96 spm. Polymorphic PVCs with some couplets, short bigeminis, isolated SVES. No AA phases, sign pause or higher grade HRST. TTE showed good systolic fiktio, concentric LVH and abnormal relaxation. Treatment for the adverse event was heparin and Marcumar (phenprocoumon); doses and routes of administration not reported. On 12-Feb-2012, the patient recovered from apoplex. Action taken with epoetin zeta was not reported. The reporter's causality assessment between the event of apoplex and epoetin zeta was not reported.

Case Comment: Overall case causality: Probably Not Consider event to be more likely due to complications of prexisting conditions given the multiple comorbidities in the medical history.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	03-FEB-2012	Activated partial thromboplastin time	47 seconds	40 20
2	07-FEB-2012	Activated partial thromboplastin	44 seconds	40

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		time		20
3	08-FEB-2012	Activated partial thromboplastin time	52 seconds	40 20
4	09-FEB-2012	Activated partial thromboplastin time	45 seconds	40 20
5	06-FEB-2012	Basophil count	0.03 Tsd/ul	0.09 0.01
6		Body height	160 CM	
7	06-FEB-2012	Differential white blood cell count	60 %	
8	06-FEB-2012	Differential white blood cell count	2 %	
9		Echocardiogram	see narrative Unknown	
10		Electrocardiogram	see narative Unknown	
11	03-FEB-2012	Electroencephalogram	see narrative Unknown	
12	06-FEB-2012	Eosinophil count	3 %	
13	06-FEB-2012	Eosinophil count	0.16 Tsd/ul	0.36 0.08
14	03-FEB-2012	Haematocrit	40 %	45.0 35.0
15	06-FEB-2012	Haematocrit	31.5 %	45.0 35.0
16	03-FEB-2012	Haemoglobin	12.5 g/dl	15.3 12.3
17	06-FEB-2012	Haemoglobin	10.0 g/dl	15.3 12.3
18	03-FEB-2012	International normalised ratio	2.12 Unknown	1.40 0.90
19	13-FEB-2012	International normalised ratio	3.04 Unknown	1.40 0.90
20	16-FEB-2012	International normalised ratio	2.52 Unknown	1.40 0.90
21	06-FEB-2012	Lymphocyte count	30 %	
22	06-FEB-2012	Lymphocyte count	1.39 Tsd/ul	3.60 1.00
23	03-FEB-2012	Mean cell haemoglobin	25.7 pg	33 27
24	06-FEB-2012	Mean cell haemoglobin	25.6 pg	33 27
25	03-FEB-2012	Mean cell haemoglobin concentration	31.3 g/dl	36 32
26	06-FEB-2012	Mean cell haemoglobin concentration	31.6 g/dl	36 32

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
27	03-FEB-2012	Mean cell volume	82 FL	96 80
28	06-FEB-2012	Mean cell volume	81 FL	96 80
29	06-FEB-2012	Monocyte count	0.50 Tsd/ul	0.54 0.08
30	06-FEB-2012	Monocyte count	5 %	
31	06-FEB-2012	Neutrophil count	3.33 Tsd/ul	6.30 2.00
32	03-FEB-2012	Platelet count	264 x10 9/l	370 180
33	06-FEB-2012	Platelet count	153 x10 9/l	370 180
34	03-FEB-2012	Prothrombin time	38 %	120 70
35	13-FEB-2012	Prothrombin time	26 %	120 70
36	16-FEB-2012	Prothrombin time	32 %	120 70
37	03-FEB-2012	Red blood cell count	4.86 Mill/ul	5.10 4.10
38	06-FEB-2012	Red blood cell count	3.88 Mill/ul	5.10 4.10
39	14-FEB-2012	Ultrasound Doppler	see narrative Unknown	
40		Weight	64 kg	
41	03-FEB-2012	White blood cell count	13.02 Tsd/ul	11.30 4.40
42	06-FEB-2012	White blood cell count	5.48 Tsd/ul	11.30 4.40
43		X-ray	see narrative Unknown	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) FERRLECIT /00345601/ (ASCORBIC ACID, FERRIC SODIUM CITRATE, FERROUS SULFATE, NICOTINAMIDE, RIBOFLAVIN, THIAMINE MONONITRATE) ; Unknown

#8) KEPPRA (LEVETIRACETAM) ; Unknown

#9) LANTUS (INSULIN GLARGINE) ; Unknown

#10) LEFLUNOMIDE (LEFLUNOMIDE) ; Unknown

#11) L-THYROXIN HENNING (LEVOTHYROXINE SODIUM) ; Unknown

#12) MIRTAZAPIN-BIOMO (MIRTAZAPINE) ; Unknown

#13) NOVALGIN /00169801/ (CAFFEINE, PARACETAMOL, PROPYPHENAZONE) ; Unknown

#14) RANITIC (RANITIDINE HYDROCHLORIDE) ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#15) SERTRALIN /01011401/ (SERTRALINE) ; Unknown

#16) SIMVASTATIN (SIMVASTATIN) ; Unknown

#17) TORASEMID AL (TORASEMIDE) ; Unknown

#18) ZOPICLONE TEVA (ZOPICLONE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient had previous history of smoking, chronic nicotine abuse,and chronic alcohol abuse to Jan 2008. Allergies wee not reported.
Unknown to Ongoing	Relevant Med History	Nephrosclerosis (Nephrosclerosis);
Unknown to Ongoing	Relevant Med History	Seizures cerebral (Seizure); Feb 2012
Unknown to Ongoing	Relevant Med History	Chronic pancreatitis (Pancreatitis chronic);
Unknown to Ongoing	Relevant Med History	Constipation chronic (Constipation); under phosphate therapy
Unknown to Ongoing	Relevant Med History	Kidney failure chronic (Chronic kidney disease); stage III-IV
Unknown to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus); out of control Feb 2009:changed to insulin
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy); DDG-stage 2b (formal, no retinopathy)
Unknown to Ongoing	Relevant Med History	Hypothyroidism (Hypothyroidism); status post thyroidectomy for benign nodes
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia); since 1999
Unknown to Ongoing	Relevant Med History	Ischemic stroke (Ischaemic stroke); right Sept 2011, Feb 2012 Re-stroke
Unknown to Ongoing	Relevant Med History	Metabolic acidosis (Metabolic acidosis);
Unknown to Ongoing	Relevant Med History	Portal hypertension (Portal hypertension);
Unknown to Ongoing	Relevant Med History	Renal anaemia (Nephrogenic anaemia);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown to Ongoing	Relevant Med History	Endarterectomy (Endarterectomy);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	right Sep 2011	
Unknown to Ongoing	Relevant Med History	Vitamin D deficiency (Vitamin D deficiency);
Unknown	Relevant Med History in 2000 in sepsis	Acute renal failure (Acute kidney injury);
Unknown	Relevant Med History in 2000	Adrenal hypofunction (Adrenal insufficiency);
Unknown	Relevant Med History	Anxiety (Anxiety);
Unknown	Relevant Med History Sep 2011 and Feb 2012	Apoplexy (Cerebrovascular accident);
Unknown	Relevant Med History start date Feb 2012; intermittent	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Cholecystolithiasis (Cholelithiasis);
Unknown	Relevant Med History until Jan 2008	Alcohol abuse chronic (Alcohol abuse);
Unknown	Relevant Med History	Depression (Depression);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Cerebrovascular infarction (Cerebral infarction);
Unknown	Relevant Med History Gastro April 08	Reflux oesophagitis (Gastrooesophageal reflux disease);
Unknown	Relevant Med History	Rhabdomyolysis (Rhabdomyolysis);
Unknown	Relevant Med History 1999	Anterior myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History 1968 for symptomatic cholecystolithiasis (+ bile duct revision)	Cholecystectomy (Cholecystectomy);
Unknown	Relevant Med History	Portal vein thrombosis (Portal vein thrombosis);
Unknown	Relevant Med History both sides Nov 08, TEP right (left May 09)	Osteonecrosis (Osteonecrosis);
Unknown	Relevant Med History	Thyroidectomy (Thyroidectomy);
Unknown	Relevant Med History Risk Factor - chronic	Nicotine abuse (Tobacco abuse);
Unknown	Relevant Med History	Smoker (Tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	APR	1940	72 Years	Female	49.50 kg	11	MAY	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Peripheral artery occlusive disease [Peripheral arterial occlusive disease]
Infection [Infection]

Case Description: This is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). A serious spontaneous report from Germany describing a case of peripheral
artery occlusive disease.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 20-DEC-2012
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 0L184M0; Exp.Dt. 01-SEP-2012}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3 per week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMINEURIN (AMITRIPTYLINE HYDROCHLORIDE) Tablet ; Unknown
#2) ARAVA (LEFLUNOMIDE) Tablet ; 06-JUN-2008 / Unknown
#3) ASS (ACETYLSALICYLIC ACID) ; 18-MAY-2011 / Unknown
#4) CALCORT (DEFLAZACORT) Tablet ; 06-JUN-2008 / Unknown
#5) CARENAL (BIOTIN, FOLIC ACID, NICOTINIC ACID, PANTOTHE
#6) METOPROLOLSUCCINAT AL (METOPROLOL SUCCINATE) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1357498

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-DEC-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case from a physician describes a 72-year-old female patient who started treatment with epoetin zeta (subcutaneous, 3 per week, batch number 0L184M0, dose not reported) for renal anemia on an unknown day in May 2012. Medical history included ischemic heart disease in February 2011 and peripheral arterial disease in May 2011; both conditions still ongoing. The patient also started hemodialysis on an unknown date. The patient was not exposed to any other erythropoetin-stimulating agent and the patient did not experience any thrombolytic event during treatment with any other erythropoetin-stimulating agent. Concomitant medications included cinacalcet (30 mg, 1x) for hyperparathyroidism; deflazacort (6 mg, 1x) and leflunomide (10 mg, 1x) for CP ; simvastatin (40 mg, 1x), clopidogrel (75 mg, 1x), and ASS (aspirin; 100 mg, 1x) for CHD . On an unknown day in May 2012, the patient (weight 53 kg; height 165 cm) started treatment with epoetin zeta. On 11-May-2012, the patient was hospitalized due to peripheral arterial disease (necrosis of left toes 2 and 4). The patient underwent a by-pass operation (amputation of left toes 2 and 4) to treat the adverse reaction. It was reported that the last dose of epoetin zeta prior to the event was on 09-May-2012. However, it was also reported that the patient received her 2nd mean dose (not specified) on 11-May-2012. It was also reported that there had been no change in dose within 3 months prior to event. Baseline laboratory data included leukocytes at 10.04 x 10^3/mcl (normal value: 4.8 - 10.8 x 10^3/mcl), erythrocytes at 3.22 x 10^6/mcl (normal value: 4.2 - 5.4 x 10^6/mcl), haemoglobin at 9.3 g/dl (normal value: 12.0 - 16.0 g/dl), haematocrit at 0.32 (unit not reported; normal value: 0.37 - 0.52), MCV at 100.0 fl (normal value: 81.0 - 99.0 fl), MCH at 28.9 pg (normal value: 28.0 - 32.0 pg), MCHC at 28.9 g/dl (normal value: 32.0 - 36.0 g/dl), and thrombocytes at 541 x 10^3/mcl (normal value: 130 - 450 x 10^3/mcl) on 20-Feb-2012; leukocytes at 7.87 x 10^3/mcl, erthrocytes at 3.11 x 10^6/mcl, haemoglobin at 8.9 g/dl, haematocrit at 0.31 (unit not reported), MCV at 98.4 fl, MCH at 28.6 pg, MCHC at 29.1 g/dl, and thrombocytes at 501 x 10^3/mcl on 26-Mar-2012; leukocytes at 8.62 x 10^3/mcl, erthrocytes at 3.33 x 10^6/mcl, haemoglobin at 9.7 g/dl, haematocrit at 0.32 (unit not reported), MCV at 96.3 fl, MCH at 29.1 pg, MCHC at 30.2 g/dl, and thrombocytes at 531 x 10^3/mcl on 23-Apr-2012. On 16-Jul-2012, laboratory tests showed leukocytes at 7.22 x 10^3/mcl, erthrocytes at 2.79 x 10^6/mcl, haemoglobin at 8.1 g/dl, haematocrit at 0.26 (unit not reported), MCV at 94.1 fl, MCH at 29.0 pg, MCHC at 30.9 g/dl, and thrombocytes at 575 x 10^3/mcl. The outcome of the event of peripheral artery occlusive disease was not recovered. The patient was discharged from the hospital on 23-May-2012. Action taken with epoetin zeta was not reported. The reporter's causality assessment of the event of peripheral arterial disease in relation to epoetin zeta was not related. English translation of the discharge letter was received on 30-Jul-2012. Follow-up report created to reflect new information regarding patient history, adverse event laboratory tests and diagnostic procedures. Diagnosis and secondary diagnoses of the patient included the following: Peripheral arterial occlusive disease stage IV (left side of the thigh and lower leg type with toe and heel lesions), postoperative wound healing disorder on left groin and left forefoot, forefoot phlegmon with lymphangitis (left), chronic renal failure with dialysis requirement, mitral insufficiency (mitral regurgitation) grade I - II, (coronary heart disease) NSTEMI on July 2011, stent in RIVA (ramus interventricularis anterior), chronic obstructive pulmonary disease grade I, degenerative lumbar syndrome (condition after fusion surgery L4 to S1), seropositive chronic polyarthritis, hyperuricemia, secondary hyperparathyroidism, and renal anemia. Diagnostic procedures included thorax x-ray (standing p.a. inspiration) on 14-May-2012 which was compared with several previous medical examinations (last one on 04-Nov-2011) and MRT-A of pelvis and leg (no preliminary study for comparison) on 15-May-2012. The results of the thorax x-ray showed diaphragm sharply and smoothly defined on both sides, raised right dome of diaphragm, both diaphragm angles are still free, regressive streaky densities inferior to the hilum on both sides, no patchy areas of increased density, peripheral and central vessels well defined, narrow upper mediastinum, cardiomegaly, unchanged position of the tip of the Shaldon catheter. In the course, there was regressive dystelectases on both sides inferior to the hilum, no signs of congestion, and no infiltrates with the cardiomegaly. The results of MRT-A of pelvis and leg showed the right renal artery not completely depicted (as far as no-flow relevant stenosis of the left renal artery). There was a regular representation of the iliac arteries without severe stenosis. Right leg: moderate atherosclerotic changes of the superficial femoral artery, atherosclerotic plaques on the P1 segment of the popliteal artery, departure stenosis of the anterior tibial artery (ATA), although still good distal contrast, continuous anterior tibial artery and fibular artery. Left leg: moderate stenosis of the superficial femoral artery and multiple stenoses of the popliteal artery, three-vessel supply to the lower leg due to the severe distal stenosis of the ATA. The assessment was: moderate atherosclerotic-related stenosis of left popliteal artery and superficial femoral artery, severe stenoses of the distal left-sided ATA, percutaneous transluminal angioplasty (PTA) recommended. Laboratory data on 11-May-2012 included increased leucocytes at 10.91 x 10^3/mcl, decreased MCHC (mean corpuscular haemoglobin concentration) at 31.1 g/dl, increased thrombocytes at 646 x 10^3/mcl, increased PTT (Partial Thromboplastin Time) at 32.6 seconds; erythrocytes at 4.42 x 10^6/mcl, haemoglobin at 13.3 g/dl, haematocrit at 0.43, MCV (Mean Corpuscular Value) at 96.7 fl, MCH (Mean Corpuscular Haemoglobin) at 30.1 pg, Quick's value at 91%, INR (International Normal Ratio) at 1.05 (unit not reported (all within normal levels). Laboratory data on 20-Jun-2012 included decreased erythrocytes at 2.97 x 10^6/mcl, decreased haemoglobin at 8.7 g/dl, decreased haematocrit at 0.28 (unit not reported), decreased MCHC at 31.4 g/dl, increased thrombocytes at 512 x 10^3/mcl; leucocytes at 8.29 x 10^3/mcl, MCV at 93.2 fl, and MCH at 29.3 (all within normal levels). Treatment and course: The inpatient admission of the patient was due to a PAOD (peripheral arterial occlusive disease) stage IV, left side. The patient reported pain at rest, redness and swelling of the left foot for 2 weeks and open areas on all toes for 1 month. Pulse status at admission included: positive pulse on both right and left common femoral artery, positive pulse on right popliteal artery but negative on the left, negative pulse on both right and left posterior tibial artery and negative pulse on both right and left dorsalis pedis artery. Doppler occlusion blood pressure at admission: RR systemic (110 mmHg), a.t.p. right and left was >200, and a.d.p. right and left was also >200. In the clinical angiological study, small ulcers covered with fibrin were detected, which were very painful on pressure, with a diameter of about 4 to 5 mm on all toes on the left side. A superficial lesion on the lateral area of the heel was also observed, which was very painful on pressure. Therapy for the adverse event

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

included diagnostic angiography of pelvis and leg on 15-May-2012, placement of a femoro-femoralen (arteria femoralis communiss-on arteria femoralis superfizialis bypass) 6mm PTFE left, intraoperative balloon angioplasty of the truncus tibiofibularis, of the arteria tibialis anterior, and of the arteria dorsalis pedis (left), left foot wound revision on 21-May-2012, forefoot revision with amputation of the big toe and of D2 and D4 toes, joint resection, V metatarsophalangeal joint, left heel revision on 31-May-2012, wound revision on left groin, swab collection, placement of a vacuum seal, forefoot revision left with further resection of metatarsal bones 1 and 5, wound revision D1 on 06-Jun-2012, muscle flap surgery with sartorius muscle left groin and vacuum sealing on 12-Jun-2012, mesh graft transplantation in the left groin with donor site from the left thigh, vacuum sealing on the groin on 18-Jun-2012, antibiotic therapy with vancomycin, and physiotherapy.
After appropriate preparation, the above operation was carried out on 21-May-2012. The Redon drains were removed in a timely manner. Due to unsatisfactory healing of the forefoot, foot revisions were carried out twice. Because of the wound healing disorders on the left groin, a wound revision with vacuum sealing took place on 06-Jun-2012. To begin with, on 12-Jun-2012, a muscle flap surgery with sartorius muscle was carried out on the left heel. In view of the satisfactory healing of the wound on the left groin, on 18-Jun-2012, a mesh graft skin transplantation was performed. Pulse status at discharge included: positive pulse on both right and left common femoral artery, positive pulse on both right and left popliteal artery, negative pulse on both right and left posterior tibial artery, positive pulse on right dorsalis pedis artery, and negative pulse on the left dorsalis pedis artery. The Doppler occlusion pressure measurement showed semisclerotic values above 200 mmHg for all foot areas. At the time of discharge from the hospital, the wounds were showing a good healing tendency. On 23-Jun-2012, we dismissed the patient from residential treatment.
Recommendations included: regular wound insoections and daily dressing in the groin with Jelonet, Mepilex application on the donor site every 5 days, daily dressing on the left forefoot with Cutimed Sorbact and Octenisept. The physician recommended a new presentation of the patient in the vascular surgery clinic for a check up at the end of a term of 6 months after discharge under previous telephone appointment. Follow up report received from a physician on 26-Dec-2012. Follow up report was created to reflect new information regarding patient history, adverse event, laboratory tests, and concomitant medications. The patient has no known drug hypersensitivities and no history of drug dependence. Dosage form of simvastatin was film tablet and frequency was 0-0-1-0); manufacturer was Ratiopharm. Brand name of cinacalcet was Mimpara, frequency was 1-0-0-0 and dosage form was film tablet. Brand name of deflazacort was Calcort, frequency was 1-0-0-0 and dosage form was tablet). Brand name of leflunomide was Arava, frequency was 0-1-0-0, and dosage form was film tablet. Brand name of clopidogrel was Plavix, frequency was 1-0-0-0, and dosage form was film tablet. Additional concomitant medications included Unizink 50 (dose not reported, 1-0-0-0, enteric-coated tablet), metoprolol succinate AL (47.5 mg, 1-0-1-0, time-release tablet), Molsihexal (8 mg, 0-0-1-0, time-release tablet), ramipril AWD (5 mg, 1-0-0-0, only on non-HD days, tablet), Tramal (dose not reported, 1-1-1-0, drops, with dosing pump), Paspertin (20 drops, as needed, x-x-x-0), Nephrotrans (840 mg, 1-0-1-0, enteric-coated tablet), Carenal (dose not reported, 1-0-0-0, film tablet), Mogadan (dose not reported, 0-0-2-0, tablet), Amineurin 25 (dose not reported, 0-0-0-1, film tablet), pantoprazole 1A Pharma (40 mg, 1-01-0, enteric-coated tablet), and HCT AL (25 mg, 1-0-0-0, tablet; roues of administration not reported, all for unknown indications. Fatal infection was added as an adverse event. The patient developed infection of the central dialysis catheter on 13-Dec-2012. Treatment included vancomycin (0.5 g, three times a week). Leukocytes on 14-Dec-2012 was 15.01 10^3/mcl (normal range: 4.8 - 10.8 10^3/mcl), 10.91 on 15-Dec-2012, 10.66 on 16-Dec-2012, 10.81 on 17-Dec-2012, 8.84 on 18-Dec-2012, and 11.20 on 20-Dec-2012. Creatinine on 14-Dec-2012 was 2.95 mg/dl (normal range: 0.50 - 0.80 mg/dl), 2.19 on 15-Dec-2012, 3.52 on 16-Dec-2012, 4.49 on 17-Dec-2012, 3.17 on 18-Dec-2012, and 4.07 on 20-Dec-2012. CRP on 14-Dec-2012 was 9.7 mg/dl (normal value: <0.5 mg/dl), 3.8 on 15-Dec-2012, 2.6 on 16-Dec-2012, 4.0 on 17-Dec-2012, 8.6 on 18-Dec-2012, and 15.1 on 20-Dec-2012. The patient died on 20-Dec-2012. Cause of death was infection. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal infection in relation to epoetin zeta was not related.

Case Comment: Overall case causality: Not related Event is not due to the suspect drug as a previous peripheral arterial disease is already present in the medical history. Overall case causality (Follow-up 13 Aug 2012): Not related No change in assessment. Overall case causality (Follow-up 08 Jan 2013): Not related New reported event of fatal infection is likewise not related as it is due to complications of catheter placement. - N. Gonzales (08 Jan 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-MAY-2012	Activated partial thromboplastin time prolonged	32.6 seconds	
2	15-MAY-2012	Angiogram	See narrative, Unknown	
3	14-DEC-2012	Blood creatinine	2.95 mg/dl	0.80 0.50
4	15-DEC-2012	Blood creatinine	2.19 mg/dl	0.80 0.50
5	16-DEC-2012	Blood creatinine	3.52 mg/dl	0.80 0.50
6	17-DEC-2012	Blood creatinine	4.49 mg/dl	0.80

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				0.50
7	18-DEC-2012	Blood creatinine	3.17 mg/dl	0.80 0.50
8	20-DEC-2012	Blood creatinine	4.07 mg/dl	0.80 0.50
9	14-DEC-2012	C-reactive protein	9.7 mg/dl	
10	15-DEC-2012	C-reactive protein	3.8 mg/dl	
11	16-DEC-2012	C-reactive protein	2.6 mg/dl	
12	17-DEC-2012	C-reactive protein	4.0 mg/dl	
13	18-DEC-2012	C-reactive protein	8.6 mg/dl	
14	20-DEC-2012	C-reactive protein	15.1 mg/dl	
15	14-MAY-2012	Chest X-ray	See narrative, Unknown	
16		Directional Doppler flow tests	see narrative, Unknown	
17	14-DEC-2012	Directional Doppler flow tests		
18	20-FEB-2012	Haematocrit	0.32, Unknown	0.52 0.37
19	26-MAR-2012	Haematocrit	0.31, Unknown	0.52 0.37
20	23-APR-2012	Haematocrit	0.32, Unknown	0.52 0.37
21	11-MAY-2012	Haematocrit	0.43, Unknown	
22	20-JUN-2012	Haematocrit	0.28, Unknown	
23	16-JUL-2012	Haematocrit	0.26, Unknown	0.52 0.37
24	20-FEB-2012	Haemoglobin	9.3 g/dl	16.0 12.0
25	26-MAR-2012	Haemoglobin	8.9 g/dl	16.0 12.0
26	23-APR-2012	Haemoglobin	9.7 g/dl	16.0 12.0
27	11-MAY-2012	Haemoglobin	13.3 g/dl	
28	20-JUN-2012	Haemoglobin	8.7 g/dl	
29	16-JUL-2012	Haemoglobin	8.1 g/dl	16.0 12.0
30		Heart rate	See narrative, Unknown	
31	11-MAY-2012	International normalised ratio	1.05, Unknown	
32	20-FEB-2012	Mean cell haemoglobin	28.9 pg	32.0 28.0

Mfr. Control Number: 1357498

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33	26-MAR-2012	Mean cell haemoglobin	28.6 pg	32.0 28.0
34	23-APR-2012	Mean cell haemoglobin	29.1 pg	32.0 28.0
35	20-JUN-2012	Mean cell haemoglobin	29.3 pg	
36	16-JUL-2012	Mean cell haemoglobin	29.0 pg	32.0 28.0
37	20-FEB-2012	Mean cell haemoglobin concentration	28.9 g/dl	36.0 32.0
38	26-MAR-2012	Mean cell haemoglobin concentration	29.1 g/dl	36.0 32.0
39	23-APR-2012	Mean cell haemoglobin concentration	30.2 g/dl	36.0 32.0
40	11-MAY-2012	Mean cell haemoglobin concentration	31.1 g/dl	
41	11-MAY-2012	Mean cell haemoglobin concentration	30.1 pg	
42	20-JUN-2012	Mean cell haemoglobin concentration	31.4 g/dl	
43	16-JUL-2012	Mean cell haemoglobin concentration	30.9 g/dl	36.0 32.0
44	20-FEB-2012	Mean cell volume	100.0, FL	99.0 81.0
45	26-MAR-2012	Mean cell volume	98.4, FL	99.0 81.0
46	23-APR-2012	Mean cell volume	96.3, FL	99.0 81.0
47	11-MAY-2012	Mean cell volume	96.7, FL	
48	20-JUN-2012	Mean cell volume	93.2, FL	
49	16-JUL-2012	Mean cell volume	94.1, FL	99.0 81.0
50	20-FEB-2012	Platelet count	541 x 10^3/mcl, Unknown	450 130
51	26-MAR-2012	Platelet count	501 x 10^3/mcl, Unknown	450 130
52	23-APR-2012	Platelet count	531 x 10^3/mcl, Unknown	450 130
53	11-MAY-2012	Platelet count	646 x 10^3/mcl, Unknown	
54	20-JUN-2012	Platelet count	512 x 10^3/mcl, Unknown	
55	16-JUL-2012	Platelet count	575 x 10^3/mcl, Unknown	450 130

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
56	11-MAY-2012	Prothrombin time	91 %	
57	20-FEB-2012	Red blood cell count	3.22 x 10^6/mcl, Unknown	5.4 4.2
58	26-MAR-2012	Red blood cell count	3.11 x 10^6/mcl, Unknown	5.4 4.2
59	23-APR-2012	Red blood cell count	3.33 x 10^6/mcl, Unknown	5.4 4.2
60	11-MAY-2012	Red blood cell count	4.42 x 10^6/mcl, Unknown	
61	20-JUN-2012	Red blood cell count	2.97 x 10^6/mcl, Unknown	
62	16-JUL-2012	Red blood cell count	2.79 x 10^6/mcl, Unknown	5.4 4.2
63	20-FEB-2012	White blood cell count	10.04 x 10^3/mcl, Unknown	10.8 4.8
64	26-MAR-2012	White blood cell count	7.87 x 10^3/mcl, Unknown	10.8 4.8
65	23-APR-2012	White blood cell count	8.62 x 10^3/mcl, Unknown	10.8 4.8
66	11-MAY-2012	White blood cell count	10.91 x 10^3/mcl, Unknown	
67	20-JUN-2012	White blood cell count	8.29 x 10^3/mcl, Unknown	
68	16-JUL-2012	White blood cell count	7.22 x 10^3/mcl, Unknown	10.8 4.8
69	14-DEC-2012	White blood cell count	15.01, X10**3/MCL	10.8 4.8
70	15-DEC-2012	White blood cell count	10.91, X10**3/MCL	10.8 4.8
71	16-DEC-2012	White blood cell count	10.66, X10**3/MCL	10.8 4.8
72	17-DEC-2012	White blood cell count	10.81, X10**3/MCL	10.8 4.8
73	18-DEC-2012	White blood cell count	8.84, X10**3/MCL	10.8 4.8
74	20-DEC-2012	White blood cell count	11.20, X10**3/MCL	10.8 4.8

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#5) CARENAL (BIOTIN, FOLIC ACID, NICOTINIC ACID, PANTOTHENIC ACID, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, SELENIUM, THIAMINE HYDROCHLORIDE, TOCOPHEROL, VITAMIN B12 NOS) Tablet ; Unknown

#7) MIMPARA (CINACALCET HYDROCHLORIDE) Tablet ; 10-FEB-2012 / Unknown

#8) MOGADAN (NITRAZEPAM) Tablet ; Unknown

#9) MOLSIHEXAL (MOLSIDOMINE) Tablet ; Unknown

#10) NEPHROTRANS (SODIUM BICARBONATE) Tablet ; Unknown

#11) PANTOPRAZOL 1A PHARMA (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#12) PASPERTIN /00041902/ (METOCLOPRAMIDE HYDROCHLORIDE) ; Unknown

#13) PLAVIX (CLOPIDOGREL BISULFATE) Tablet ; 18-MAY-2011 / Unknown

#14) SIMVASTATIN RATIOPHARM (SIMVASTATIN) Tablet ; 18-MAY-2011 / Unknown

#15) TRAMAL (TRAMADOL HYDROCHLORIDE) ; Unknown

#16) UNIZINK (ASPARTATE ZINC) Tablet ; Unknown

#17) HCT (HYDROCHLOROTHIAZIDE) Tablet ; Unknown

#18) RAMIPRIL (RAMIPRIL) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Follow up report received on 26-Dec-2012: The patient has no known drug hypersensitivities and no history of drug dependence. The patient died on 20-Dec-2012. Cause of death was infection. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History February 2011	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease); May 2011; left side of thigh and lower leg type with toe and heel lesions
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Grade I	Chronic obstructive pulmonary disease (Chronic obstructive pulmonary disease);
Unknown	Relevant Med History	Lumbar spine degeneration (Spinal osteoarthritis); condition after fusion surgery L4 to S1
Unknown	Relevant Med History	Back pain (Back pain);
Unknown	Relevant Med History	Lymphangitis (Lymphangitis);
Unknown	Relevant Med History	Phlegmon (Cellulitis);
Unknown	Relevant Med History	Spinal fusion surgery (Spinal fusion surgery);
Unknown	Relevant Med History	Hyperuricemia (Hyperuricaemia);
Unknown	Relevant Med History Grade I - II	Mitral insufficiency (Mitral valve incompetence);
Unknown	Relevant Med History Grade I - II	Mitral regurgitation (Mitral valve incompetence);
Unknown	Relevant Med History	Non STEMI (Acute myocardial infarction);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	July 2011	
Unknown	Relevant Med History	Impaired healing (Impaired healing);
Unknown	Relevant Med History	Renal anaemia (Nephrogenic anaemia);
Unknown	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown	Relevant Med History	Chronic polyarthritis (Polyarthritis);
Unknown	Relevant Med History	Stent placement (Stent placement);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	08	MAY	1929	82 Years	Female	57.00 kg		FEB	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplex insult [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer-sponsored Post-Authorization Safety Cohort Observation (PASCO), protocol EPOE-09-11, regarding subject 1150001.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 2000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 27-OCT-2010 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) APROVEL (IRBESARTAN) ; Ongoing
#2) BISOPROLOL (BISOPROLOL) ; Ongoing
#3) DIGITOXIN (DIGITOXIN) ; Unknown
#4) MARCUMAR (PHENPROCOUMON) ; Ongoing
#5) TOREM (TORASEMIDE) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1393463

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-AUG-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 82-year-old female subject started to receive epoetin zeta (RETACRIT) 2000 IU subcutaneously weekly (independent value of mean dose) on 27Oct2010 for the treatment of renal anemia. The dose was not changed within 3 months prior to the event. The last dose of the study drug before event was reported to be given on 27Oct2010. Hemoglobin under "mean dose 1 (2000)"- 12.2; under "mean dose 2 (2000)"- 12.9. Her medical history was significant for hypercalcemia since 01Jun2011, atrial fibrillation, hyperlipidemia, hypertension, ischemic heart disease, and a cardiac pacemaker insertion since Nov2009, all reported as ongoing. Medical records showed that the subject had examination on 11May2011. It was reported that the subject was not on dialysis. The subject had previously used epoetin beta/ methoxy polyethylene glycol (MIRCERA) 190 mg/mg/week from 06Oct2009 to Sep2010 and then until 27Oct2010 at 50 ug/week (hemoglobin- 12,7). There were no thromboembolic events under treatment with other erythropoetin-stimulating medications. Concomitantly she was on irbesartan (APROVEL) 300 mg once daily, bisoprolol 10 mg once daily, and torasemide (TOREM) 10 mg twice daily, all 3 for hypertension; and phenprocoumon (MARCUMAR) dose according to Quick's test for atrial fibrillation, all ongoing, and digitoxin 0.07 (unspecified units) once daily for atrial fibrillation. On an unspecified date, the subject's hemoglobin was 13.0 g/dL. On an unknown day in Feb2012, she experienced apoplex insult involving transient ischemic attack (TIA) and dysarthria. She was hospitalized and was treated with heparin. Diagnoses included currently stable cardiac insufficiency; hypertensive cardiac disease with atrial fibrillation and valve insufficiencies; state after pacemaker implantation due to atrial fibrillation and bradycardic chamber action; state after cardiac decompensation; aortic valve stenosis ("low grade stenosis"?), increase of pressure gradients (max. 70 mmHg); goiter, hyperthyroidism under disseminated autonomy, state after radioactive iodine therapy; permanent anticoagulation; dizziness with instable gait. Tests on unspecified dates include body mass index (BMI) 27.5; hemoglobin 13.1 mg/dl, 13 mg/dl, 12.9 mg/dl, 12.2 mg/dl, 12.5 mg/dl (normal range 12-16 mg/dl); hemoglobin 13 g/dl, 12.2 g/dl, 12.9 g/dl, 12.7 g/dl; hematocrit 39.7%, 38.6%, 38.4%, 37.4%, 37.4% (normal range 36-47%); red blood cell count (RBC) 4.36 x10^12/l, 4.31 x10^12/l, 3.98 x10^12/l, 4.04 x10^12/l, 4.22 x10^12/l (normal range 3.9-5.4 x10^12/l); C-reactive protein (CRP) 63.07, 8.74, 15.38, 16.55, 19.38 (normal range <5); white blood cell count (WBC) 14.59 x10^9/l, 10.06 x10^9/l, 11.78 x10^9/l, 10.71 x10^9/l, 12.04 x10^9/l (normal range 3.6-9.6 x10^9/l). Physical examination showed discrete ankle edemas, spider veins. ECG in rest: basic rhythm atrial fibrillation, regular pacemaker actions only (VVI), chamber frequency 72 QRS/min, no ventricular events. Color doppler echocardiography: cardiac dilatation at the atrial level, no increase of left ventricular enddiastolic diameter, moderately restricted LV function under concetric hypertrophy, pericardic separation in front of the right atrium. No progression of AV valves insufficiencies, mild- to moderate mitral valve insufficiency. Pronounced regurgitation with wide reflux signal over tricuspidal valve , systelic PA pressure is unchanged at approx. 50 mmHg. Aortal valve docked tricuspidally, remarkably fibrosed, complicated planimetry, aortic valve area at approx. 0.6 cm2, maximal pressure gradient now at 70 mmHg, increasing. Summary assessment: stable situation, despite progression of aortic valve stenosis, BNP value decreases. Retention readings decreased in comparison to previous examinations. The subject does not wish for any further diagnostic or therapeutic measures. Echocardiographic control was recommended in 3 months. The action taken with epoetin zeta in response to the event was unknown. The subject recovered and was discharged from the hospital on an unknown day in Feb2012. The reporter's assessed the causality for the event of apoplex insult in relation to epoetin zeta as not related.

Follow-up (29Jun2017): Updates medical history, concomitant medications, study drug dose, tests.

Follow-up (31Jul2017): Updates subject's details, study drug start date and details, tests.

Follow-up (08Aug2017): Updates last dose before event.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the event was related to study medication. The event was most likely due to natural pathophysiology of apoplexy given the patient's age and multiple risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body mass index	27,5	
2		C-reactive protein	19,38	5
3		C-reactive protein	16,55	5
4		C-reactive protein	15,38	5
5		C-reactive protein	8,74	5
6		C-reactive protein	63,07	5
7		Electrocardiogram	basic rhythm atrial fibrillation	

Mfr. Control Number: 1393463

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
8		Haematocrit	39,7 %	47 36
9		Haematocrit	38,6 %	47 36
10		Haematocrit	38,4 %	47 36
11		Haematocrit	37,4 %	47 36
12		Haematocrit	37,4 %	47 36
13		Haemoglobin	12,9 mg/dl	16 12
14		Haemoglobin	12,2 mg/dl	16 12
15		Haemoglobin	12,5 mg/dl	16 12
16		Haemoglobin	13,1 mg/dl	16 12
17		Haemoglobin	12,9 g/dl	
18		Haemoglobin	13.0 g/dl	
19		Haemoglobin	12,2 g/dl	
20		Haemoglobin	12,7 g/dl	
21		Haemoglobin	13 mg/dl	16 12
22		Red blood cell count	4,22 x10 12/l	5,4 3,9
23		Red blood cell count	4,04 x10 12/l	5,4 3,9
24		Red blood cell count	3,98 x10 12/l	5,4 3,9
25		Red blood cell count	4,31 x10 12/l	5,4 3,9
26		Red blood cell count	4,36 x10 12/l	5,4 3,9
27		Ultrasound Doppler	cardiac dilatation at the atrial level	
28		White blood cell count	10,71 x10 9/l	9,6 3,6
29		White blood cell count	11,78 x10 9/l	9,6 3,6
30		White blood cell count	10,06 x10 9/l	9,6 3,6
31		White blood cell count	14,59 x10 9/l	9,6 3,6
32		White blood cell count	12,04 x10 9/l	9,6 3,6

Mfr. Control Number: 1393463

ADDITIONAL INFORMATION

13. Relevant Tests

ECG in rest (unknown date): basic rhythm atrial fibrillation, regular pacemaker actions only (VVI), chamber frequency 72 QRS/min, no ventricular events
Color doppler echocardiography (unknown date): cardiac dilatation at the atrial level, no increase of left ventricular enddiastolic diameter, moderately restricted LV function under concetric hypertrophy, pericardic separation in front of the right atrium. No progression of AV valves insufficiencies, mild- to moderate mitral valve insufficiency. Pronounced regurgitation with wide reflux signal over tricuspidal valve , systelic PA pressure is unchanged at approx. 50 mmHg. Aortal valve docked tricuspidally, remarkably fibrosed, complicated planimetry, aortic valve area at approx. 0.6 cm2, maximal pressure gradient now at 70 mmHg, increasing.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
NOV-2009 to Ongoing	Relevant Med History	Cardiac pacemaker insertion (Cardiac pacemaker insertion);
01-JUN-2011 to Ongoing	Relevant Med History	Hypercalcemia (Hypercalcaemia);
06-OCT-2009 to 27-OCT-2010	Past Drug Event	Mircera (MIRCERA); 190 mg/mg/week from 06Oct2009 to Sep2010 50 ug/week until 27Oct2010

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	24	DEC	1935	76 Years	Female	75.00 kg	05	MAY	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

TIA [Transient ischaemic attack]

Case Description: This is a Hospira-Sponsored Post-Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of transient
ischemic attack (TIA). This serious case (reference: Ge-115-031) describes a 76-year-old female patient (Weight: 75 Kg; Height : 168 cm) who received Retacrit (epoetin zeta; subcutaneous; dose, batch number, and formulation not

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 05-SEP-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
		Allergies, alcohol consumption, and tobacco usage were not reported.
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1393560

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-AUG-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1393560

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

reported) for renal anaemia on 05-Sept-2011. Medical history included obesity, hyperlipidemia, peripheral arterial disease, and hypertension. Concomitant medications were not reported. The patient was exposed to another erythropoietin stimulating agent (ESA); Aranesp (darboepoetin alfa; dose and route of administration not reported) on 24-Nov-2008. On 05-Sept-2011, the patient began treatment with epoetin zeta. On 05-May-2012, the patient experienced TIA. On the same day, the patient was hospitalized for the adverse reaction. No dose changes were done within three months prior to the event. Action taken with epoetin zeta was not reported. The report stated that there was no treatment given for the adverse event. On 10-May-2012, hospital admission ended and the patient fully recovered from the event of TIA. The reporter's causality assessment between the event of TIA in relation to epoetin zeta was not related.

Case Comment: Overall case causality: Not related Event is more likely due to natural pathophysiology of cerebrovascular ischemia, given the patient's age and multiple risk factors.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Obesity (Obesity);
24-NOV-2008 to Unknown	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	07	JUN	1946	65 Years	Female	68.00 kg	12	JAN	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Shunt thrombosis [Shunt thrombosis]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO II) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a serious case of shunt
thrombosis. This case from a physician (reference: GE115-035) describes a 65-year-old female patient (weight: 68 kg and height: 165 cm) who received Retacrit (subcutaneous, once per week; dose, and batch number not reported) for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) Freq: 1 Week, Interval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 25-OCT-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
	Allergies, alcohol consumption, and tobaco usage were not reported.	
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1393630

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-AUG-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

renal anaemia from 28-Oct-2011 until an unknown date. Medical history included hyperlipidemia and hypertension. Past drug history included Mircera 75 (methoxy polyethylene glycol-epoetin beta) until 2011. Concomitant medications were not reported. On 28-Oct-2011, the patient started treatment with epoetin zeta. On 12-Jan-2012, the patient experienced shunt thrombosis. The adverse event required shunt revision and a surgery was planned. Action taken with suspect drug was not reported. On 17-Jan-2012, the patient recovered from the event of shunt thrombosis. The reporter's causality assessment between the event of shunt thrombosis and epoetin zeta was not related.

Case Comment: Overall case causality: Not related Event is a normal complication associated with the shunt.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Past Drug Event	MIRCERA (MIRCERA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	17	MAR	1940	72 Years	Female	58.00 kg	17	SEP	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischaemic stroke [Ischaemic stroke]

Case Description: This is a Post-Authorization Safety Cohort Observation of Retacrit (epoetin zeta) Administered Subcutaneously for the Treatment of Renal Anemia (PASCO II). This report from Italy describes a case of ischaemic stroke. This serious case
from a physician (ref: IT-038-0002) describes a 72-year-old female patient (weight: 58 Kg; height 160 cm) who received Retacrit (epoetin zeta; dose not reported, three times a week on 04-Jul-2011 and 8000 IU, twice a week on 22-Aug-2012,

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) Freq: 3 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 04-JUL-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) COUMADIN /00014802/ (WARFARIN SODIUM) ; 10-OCT-2011 / Unknown
#2) DIBASE (COLECALCIFEROL) ; 22-AUG-2011 / Unknown
#3) NORVASC (AMLODIPINE BESILATE) ; 20-FEB-2012 / Unknown
#4) PANTORC (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 04-JUL-2011 / Unknown
#5) TIKLID (TICLOPIDINE HYDROCHLORIDE) ; 12-MAR-2012 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
		Allergies, alcohol consumption, and tobacco usage were not reported.
Unknown to Ongoing	Relevant Med History	Anicteric cholestasis (Cholestasis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1438497

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

subcutaneous; batch number not reported) for renal anaemia. Medical history included peripheral arterial disease (obliterant vasculopathy) in 2011, type 2 diabetes mellitus with macrovascular and microvascular complications in 1988, hypertension in 1988, paroxysmal atrial fibrillation on oral anticoagulant therapy in Jul 2011, breast cancer resolved in 2001, and Crohn's disease in 2011, end stage renal dialysis therapy, and anicteric cholestasis induced by inflammatory stenosis of the Vater papilla. The patient was not exposed to any other erythropoeitin stimulating agent (ESA) and did not experience any thromboembolic event during the treatment with any other ESA. Concomitant medication included Coumadin (warfarin; dose varies according on the INR, once a day), Dibase (cholecalciferol; 20 drops, once a week), Tiklid (ticlodipine; 250 mg, once a day), and Pantorc (pantoprazole; 40 mg, once a day); all routes of administration not reported as prophylaxis, and Norvasc (amlodipine; 5 mg, once a day) for hypertension. On 04-Jul-2011, the patient began treatment with epoetin zeta. On 22-Aug-2012, the dose of epoetin zeta was changed 8000 IU twice a week. On 17-Sep-2012, the patient experienced ischaemic stroke ponto-mesencephalic. On 19-Sep-2012, the patient was sent to emergency department for the onset of dysarthria associated with deviation of the mouth. Upon admission, the patient was alert, oriented, and cooperative, had moderate dysarthria, and referred dysphagia for liquids, had deviation of the mouth and mild right upper limb weakness. The remaining neurological observations were normal. The patient had widespread skin discoloration, right jugular central venous catheter (CVC). The patient had hemithorax symmetrical, bases hypomobile, clear sound from entire lungs, minimal volume (MV) reduced bilaterally at bases; abdomen flat treatable, not tender nor painful, liver palpable from rib cage; hyposphygmia of peripheral pulses of lower limbs, rhythmic heart sounds, and systolic murmur of all outbreaks. The patient's blood pressure was at 180/70, heart beats at 58 R, and oxygen saturation (SO2) at 99%. On the same day, brain CAT scan was performed. The result that there were no signs of cerebro-meningeal bleeding in place; there was a hypodense area near the left front portion of the midbrain, which appeared slightly swollen. This finding was compatible with a subacute ischemic lesion. There was no evidence of other focal abnormalities of the brain parenchyma nor expansive intracranial lesions. The cerebrospinal fluid (CSF) peri-encephalic spaces and the ventricular system were slightly accentuated. Midline was in axis. There were widespread calcifications of the carotid siphons. On an unknown date, 48 hours after the control, brain CAT scan was again performed. The result showed no substantive changes in intracranial findings with respect to a previous similar examination on 19-Sep-2012 with the exception of a slightly greater emphasis of a left ponto-mesencephalic hypodensity attributable to ischemic lesion, and associated focal ponto-mesencephalic swelling. On an unknown date, blood tests were performed that showed hemoglobin (Hb) at 14.8 g/dl, mean cell volume (MCV) at 90 fl, white blood cell count (WBC) 6,220/mmc, platelet count (PLT) at 162,000/mmc, creatinine at 3.5 mg/dl, erythrocyte sedimentation rate (VES) at 76 mm/h, c-reactive protein (PCR) at 5.4 mg/dl, alanine aminotransferase(AST) at 23 U/l, alanine aminotransferase (ALT) at 21 U/l, alkaline phosphatase (ALP) at 317 U/l and 709 U/l, and gamma glutamyl transferase (y-GT) at 98 U/l. The report stated that no treatment was given for the adverse event. During recovery, the movement was recuperated in the right arm with outcomes at the level of the buccal rhyme. The dysphagia, prior to the ischemic event, was examined in-depth with a visit to the speech therapist and it appeared that specific home nutrition can be applied as indicated during counseling. During the speech consultation, it was suggested that the patient have a soft and creamy diet, hydration with gel water, tablets crushed in water gel, and avoid heterogeneous textures. The patient recovered with sequelae of deviation rhyme buccal dysarthria on an unknown date. On 25-Sep-2012, the patient was discharged from the hospital. The reporter's causality assessment between the event of ischaemic stroke and epoetin zeta was not related. 23-Jan-2014: Data entry correction was done to reflect results of brain CAT scan, neurological and physical exam in the laboratory section. Active substance name and frequencies for all concomitant medications and frequency for epoetin zeta were populated on the structured fields. Data entry correction was also done to reflect indication of warfarin, cholecalciferol, ticlodipine and pantoprazole (routes of adminstration not reported) all given as prophylaxis in the narrative.

Case Comment: Overall case causality: Not related Event is due to normal pathophysiology of ischemia given the patient's age, history of diabetes and peripheral arterial disease. Corrected report (14 Feb 2014): No change in previous company assessment. - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Alanine aminotransferase	21 IU/l	
2		Aspartate aminotransferase	23 IU/l	
3		Blood alkaline phosphatase	317 IU/l	
4		Blood alkaline phosphatase	709 IU/l	
5		Blood creatinine	3.5 mg/dl	
6	19-SEP-2012	Blood pressure measurement	180/70, Unknown	

Mfr. Control Number: 1438497

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7		C-reactive protein	5.4 mg/dl	
8		Computerised tomogram head	Attributable to ischemic lesion, Unknown	
9		Computerised tomogram head	Associated focal ponto-mesencephalic swelling, Unk	
10		Computerised tomogram head	Emphasis of left ponto-mesencephalic hypodensity,	
11		Computerised tomogram head	No substantive changes in intracranial findings,	
12	19-SEP-2012	Computerised tomogram head	No evidence focal abnormalities brain parenchyma,	
13	19-SEP-2012	Computerised tomogram head	Widespread calcifications of carotid siphons, Unk	
14	19-SEP-2012	Computerised tomogram head	No signs of cerebro-meningeal bleeding in place,	
15	19-SEP-2012	Computerised tomogram head	Midline was in axis, Unknown	
16	19-SEP-2012	Computerised tomogram head	Which appeared slightly swollen, Unknown	
17	19-SEP-2012	Computerised tomogram head	Ventricular system slightly accentuated, Unknown	
18	19-SEP-2012	Computerised tomogram head	No evidence of expansive intracranial lesions, Unk	
19	19-SEP-2012	Computerised tomogram head	Hypodense area near left front portion midbrain,	
20	19-SEP-2012	Computerised tomogram head	CSF peri-encephalic spaces slightly accentuated,	
21	19-SEP-2012	Computerised tomogram head	Compatible with a subacute ischemic lesion, Unk	
22		Gamma-glutamyltransferase	98 IU/l	
23		Haemoglobin	14.8 g/dl	
24	19-SEP-2012	Heart rate	58 R, Unknown	
25		Mean cell volume	90, FL	
26	19-SEP-2012	Neurological examination	Mild right upper limb weakness, Unknown	
27	19-SEP-2012	Neurological examination	Had deviation of the mouth, Unknown	
28	19-SEP-2012	Neurological examination	Had moderate dysarthria, Unknown	
29	19-SEP-2012	Neurological examination	Alert, oriented, and cooperative, Unknown	
30	19-SEP-2012	Neurological examination	Remaining observations	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			were normal, Unknown	
31	19-SEP-2012	Neurological examination	Referred dysphagia for liquid, Unknown	
32	19-SEP-2012	Oxygen saturation	99 %	
33	19-SEP-2012	Physical examination	Systolic murmur of all outbreaks, Unknown	
34	19-SEP-2012	Physical examination	Right jugular central venous catheter, Unknown	
35	19-SEP-2012	Physical examination	Rhythmic heart sounds, Unknown	
36	19-SEP-2012	Physical examination	Liver palpable from rib cage, Unknown	
37	19-SEP-2012	Physical examination	Hyposphygmia of peripheral pulses lower limbs, Unk	
38	19-SEP-2012	Physical examination	Abdomen flat treatable, not tender norpainful, Unk	
39	19-SEP-2012	Physical examination	Hemithorax symmetrical, bases hypomobile, Unk	
40	19-SEP-2012	Physical examination	Minimal volume reduced bilaterally at bases, Unk	
41	19-SEP-2012	Physical examination	Widespread skin discoloration, Unknown	
42	19-SEP-2012	Physical examination	Clear sound from entire lungs, Unknown	
43		Platelet count	162000/mmc, Unknown	
44		Red blood cell sedimentation rate	76 mm/h, Unknown	
45		White blood cell count	6220/mmc, Unknown	

13. Relevant Tests

Brain CAT scan: Emphasis of left ponto-mesencephalic hypodensity, Unknown
Brain CAT scan: No substantive changes in intracranial findings, Unknown
Brain CAT scan (control): CSF peri-encephalic spaces slightly accentuated, Unknown
Brain CAT scan (control): Hypodense area near left front portion midbrain, Unknown
Brain CAT scan (control): No evidence focal abnormalities brain parenchyma, Unknown
Brain CAT scan (control): No signs of cerebro-meningeal bleeding in place, Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	8000 IU, Freq: 2 Week; Interval: 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	22-AUG-2012 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Papilla of Vater stenosis (Papilla of Vater stenosis);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History recovered in 2001	Breast cancer (Breast cancer);
Unknown to Ongoing	Relevant Med History 2011	Crohn's (Crohn's disease);
Unknown to Ongoing	Relevant Med History	Dialysis (Dialysis);
Unknown to Ongoing	Relevant Med History in 1988	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History in Jul 1988	Paroxysmal atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History obliterant vasculopathy in 2011	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History in 1988	Diabetic complication (Diabetic complication);
Unknown to Ongoing	Relevant Med History in 1988	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	05	SEP	1927	85 Years	Female	94.00 kg	30	DEC	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Formally NSTEMI [Acute myocardial infarction]
Left basal pneumonia [Pneumonia]
Renal insufficiency [Renal failure]

Case Description: Fatal renal insufficiency, left basal pneumonia and formally NSTEMI. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (reference: Ge-432-0005), which refers to an 85-year-old Caucasian
female patient (height: 168 cm, weight: 94 kg).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 28-DEC-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 32 iu/kg/we (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 11-JUN-2012 / 26-DEC-2014

19. THERAPY DURATION
#1) 929 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DEKRISTOL (COLECALCIFEROL) Capsule ; 25-JUL-2010 / Unknown
#2) FERRLECIT /00345601/ (ASCORBIC ACID, FERRIC SODIUM CITR
#3) LANTUS (INSULIN GLARGINE) ; Unknown
#4) MARCUMAR (PHENPROCOUMON) ; Unknown
#5) NITROSPRAY (GLYCERYL TRINITRATE) ; Unknown
#6) NOVORAPID (INSULIN ASPART) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History 2010	Acute on chronic renal failure (Acute kidney injury)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1595758

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included hyperlipidemia, ischemic heart disease from 1999, peripheral arterial disease from 30-Dec-2012, diabetes mellitus from 1999, hypertension and atrial fibrillation. It also included thumb amputation on the left around 1963, coronary 3 vessel disease, percutaneous transluminal coronary angioplasty (PTCA) and stent in the anterior interventricular artery in 1999, permanent VHF, mitral valve insufficiency grade I and II with left atrial dilatation, hypertensive nephropathy which led to renal failure diagnosed in 29-Nov-2005. The patient had acute to chronic kidney failure in 2010 with known nephropathy and nephroangiosclerosis, intermittent haemodialysis treatment via Shaldon catheter on the right groin, diabetic polyneuropathy with cl. pressure marks DI and II on the left traumatic finger. The patient had no allergies, drug hypersensitivities, or history of drug dependence. The patient was self-sufficient, and with mobile Rollator. Successful direct stenting of a 90% without restenosis was done on 15-Aug-2008. It was also reported that the patient had no problems for the last 23 months. Past drug therapy included moxifloxazine (dose and route of administration not reported), taken by the patient up to 05-May-2010. The patient was previously treated with an erythropoiesis-stimulating agent (ESA) Aranesp (darbepoetin; mean dose: 167 mcg/week, dose also reported as 177 ng/kg/week for the last three months, route of administration not reported; from 08-Dec-2005 until 07-Jul-2012) and experienced percutaneous transluminal coronary angioplasty (PTCA) - RCX 90% STENT in Aug 2008 and lung edema (myocardial ischemia) on 23-Oct-2008. Concomitant medications included amlodipin tablet (5 mg, 1-0-1), bisoprolol tablet(2.5 mg, 1-0-0), ramipril tablet (5 mg, 1-0-0), torasemid tablet (50 mg, 1-0-0), Marcumar (according to Quick/INR), ASS tablet (100 mg, 0-1-0), Dekristol 20000 capsule (1-0-0; dose not reported, Sundays only, 1 capsule from 25-Jul-2010), Pantozol tablet (40 mg, 1-0-0), Citalopram tablet (10 mg, 0-0-1), Simvabeta tablet (40 mg, 0-0-1), Nitro spray (if needed, rarely; dose not reported), Novorapid (10-10-10 E; according to blood sugar), and Votum (20 mg, 1-0-1), routes of administration not reported; Ferrlecit (62.5 mg, intravenous infusion, once every 3 weeks), Lantus (0-0-0-14 IE, subcutaneous), all for unknown indications. On 11-Jun-2012, the patient started to receive epoetin zeta (Retacrit, lot number unknown; 32 IU/Kg/week, mean dose of 3000 U/W, also reported as 1000 E, three times a week, daily dose reported as 3000 E/7 = 430 E; subcutaneous, solution for injection in pre-filled syringe) for renal anaemia. It was reported that the patient received the suspect drug regularly without problem, as self-injection. On 02-Jul-2012, the patient also received epoetin zeta. On 12-Dec-2012, the patient was enrolled in the study. Laboratory tests done on 17-Dec-2012 revealed creatinine at 2.71 mg/dl, erythropoetin at 4.22 Mill/mcl, hemoglobin at 12.20 g/dl, hematocrit at 36 %, INR at 2.90 kA, potassium at 4.10 mmol/L, quick test at 23 %, and thrombocytes at 201 Tsd/mcl (normal values not reported). On 28-Dec-2012, the patient received the last dose of epoetin zeta prior to onset of the event. On 30-Dec-2012, the patient experienced left basal pneumonia; formally NSTEMI and was hospitalised. The adverse event was also described as febrile pulmonary affection. It was reported that on that day, the patient woke around 4 am and vomited. She felt pain from the left shoulder to the right shoulder, but this was a frequent occurrence. The patient vomited around 6 times. The patient's temperature that morning was 38.2 degrees Celsius. The patient had a frequent cough recently, with yellow expectorant. On an unknown date, the patient experienced renal insufficiency. Upon admission, the patient was in reduced general health, with adipose nutritional status. On examination, the blood pressure was at 186/73 mmHg, pulse was at 121/min, respiratory rate was at 27/min, oxygen saturation was at 94%, and temperature was at 37.2 degrees Celsius (normal values not reported). The patient's pulmonary had vesicular respiratory sounds, left basal quiet fine bubble rattling. Heart tones were pure and arrhythmic. Abdomen was without muscular guarding, pressure pain or resistance. Liver and spleen were not enlarged upon examination by palpation. Renal bed was not painful to touch. The patient had discrete lower leg edema on both sides, varicosis. The patient had ulcer D1 plantar on the left, right D1 medial dry necrosis. On 30-Dec-2012, thoracic X-ray revealed cardiomegaly, chronic pulmonary vascular congestion, left basal increased streaking (potential incipient infiltrate). Electrocardiogram (ECG) done on the same day revealed VHF, frequency 121/min, right axis deviation, loss of R-waves via the front wall, discrete ST depression V4-V6, T negative in II, III, aVF. On 31-Dec-2012, ECG revealed VHF, 84/min, RT, incompl. RBBB, Av block I, T-neg in V5-V6. The patient received in-patient treatment with elevated Troponin-T. In response to the adverse event, the patient also received treatment with Rocephin (2 g, intravenous) then cefuroxime (250 mg, oral). Laboratory tests done on 02-Jan-2013 revealed cholesterol at 126 mg/dl (normal values:120-200), triglyceride at 95 mg/dl (normal values: 55-200), HDL cholesterol at 49 mg/dl (normal values: above 45), HDL/cholesterol quotient at 39% (normal values: above 20), LDL cholesterol nFW at 58 mg/dl (normal values: below 155), creatinine at 2.1 mg/dl (normal values: 0.5-0.9), urea at 133 mg/dl (normal values: 10-50), uric acid at 11.3 mg/dl (normal values: 2.5-6.8), creatinine kinase (CK) at 81 U/l (normal values up to 170), troponin T at 384 pg/ml (normal values less than 14), C-reactive protein (CRP) at 3.7 mg/dl (normal values at 0.1-0.6), leukocytes at 8 x 10^3/mcl (normal values: 4-12), banded granulocytes at 0.18 x 10^3/mcl (normal values: 0-0.70), segmented granulocytes at 5.90 x 10^3/mcl (normal values: 1.8-7.7), eosinophile granulocytes at 0.39 x 10^3/mcl (normal values: 0-0.45), basophile granulocytes at 0.03 x 10^3/mcl (normal values:0-0.20), lymphocytes at 1.02 x 10^3/mcl (normal values: 1-4.8), monocytes at 0.38 x 10^3/mcl (normal values: 0-0.8), thrombocytes at 195 x 10^3 mcl (normal values: 100-350), Quick's test at 61% (normal values: 70-130), and partial thromboplastin time (PTT) at 27 sec (normal values: less than 40). Findings on the echocardiogram done on 02-Jan-2013 included hypertensive heart disease with normal left ventricular pump function, EF 57%, mild aortic stenosis, mitral ring sclerosis, mild tricuspid insufficiency with severe pulmonary artery hypertension, and CHD. Laboratory tests done on 03-Jan-2013 revealed pH value at 7.47 (unit not reported) (normal values: 7.37-7.44), pCO2 at 27.6 mmHg (normal values: 35-45), bicarbonate (HCO3) at 19.5 mmol/l (normal values: 20-28), base excess at -2.7 mmol/l (normal values: 0 plus/minus 3), pO2 at 70 mmHg (normal values: 71-104), oxygen saturation at 95 % (normal values not reported). Laboratory results formally indicated a NSTEMI 'without accompanying clinic and a conservative process was indicated. During the course of the antibiotic treatment, there was significant improvement of clinical symptoms and

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

decrease in inflammatory parameters. As a result of Marcumar treatment and a Quick value of 35% on 04-Jan-2013, the patient was recommended to be administered with Marcumar on Jan 4, 5, and 6, 2013. Laboratory tests done on 04-Jan-2013 also revealed international normal ratio (INR) at 2.61 (normal values: 2-3). On 07-Jan-2013 (Monday), Quick's test monitoring was requested and adjustment of the administration was to be done if necessary. On 04-Jan-2013, the patient recovered from the event of pneumonia; formally NSTEMI and was discharged from the hospital. Treatment for the adverse event of renal insufficiency was not reported. The suspect drug was discontinued on 26-Dec-2014. The patient died on 28-Dec-2014. Cause of death was renal insufficiency. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of left basal pneumonia; formally NSTEMI in relation to epoetin zeta was unlikely. It was reported that the event of fatal renal insufficiency was of no relation to Retacrit. The patient's risk factors included obesity (33.3), coronary heart disease, atrial fibrillation, hypertension, diabetes type 2 with no diabetic vascular complications, and heart failure NYHA stage II. 14-Feb-2013: English translation of the discharge letter was received. The reported adverse event term pneumonia was changed to left basal pneumonia. Additional medical history was provided. Moxifloxazine was added as past drug therapy. ECG, x-ray, echocardiogram, cholesterol, triglyceride, HDL cholesterol, HDL/cholesterol quotient, LDL cholesterol, creatinine, urea, uric acid, creatinine kinase, C-reactive protein, leukocutes, banded granulocytes, segmented granulocytes, eosinophine granulocytes, basophile granulocytes, lymphocytes, monocytes, thrombocytes, partial thromboplastin time, pH, pCO2, bicarbonate, base excess, pO2, and oxygen saturation were added as diagnostic and laboratory tests. Adverse event and admission details were also provided. These information were reflected in the narrative and in the corresponding data fields. 02-Feb-2015: Additional information was received from the reporter. Sudden death at home was added as adverse event. Coronary heart disease, atrial fibrillation, hypertension, diabetes type 2 with no diabetic vascular complications, and heart failure NYHA stage II were added as risk factors, and hypertensive nephropathy was added as medical history. The patient was not on dialysis. Active substance name and other dose were provided for Aranesp. The patient's date of enrollment and the dose and frequency of epoetin zeta during the week of entry were provided. Death details were also provided. Data entry corrections were made to correct the MedDRA code of mitral valve insufficiency (instead of mitral valve incompetence); myocardial ischemia, direct stenting and permanent VHF were coded in the medical history section. This information was reflected in the narrative and in the corresponding data fields. 09-Feb-2015: Additional information was received from the same reporter. It was reported that the patient had no known drug hypersensitivities or drug dependence and had no problems for the last 23 months. Dosage forms for amlodipine, bisoprolol, ASS, Pantozol, Citalopram, and Simvabeta were all reported as tablet. It was stated that dose of Marcumar was according to Quick/INR while dose of Novorapid was according to blood sugar. Frequency of Nitro spray was further described as rarely. Votum was added as concomitant medication. Therapy start date and therapy end date of suspect drug Retacrit were updated; daily dose was also provided. It was reported that the patient received the suspect drug regularly without problem, as self-injection. Action taken with the suspect drug and reporter's causality assessment for the event of sudden death at home were provided. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit (epoetin zeta): Batch number and date of expiry. Data entry correction was also made to reflect the cause of death as unknown cause of death in the data field and to reflect the dosage form of Dekristol as capsule. This information has been incorporated in the narrative and in the corresponding data fields. 21-Apr-2015: Additional information received from the same reporter to update cause of death and to add fatal renal insufficiency as an event. This information has been incorporated in the narrative and corresponding data fields.

Amendment: This follow-up report is being submitted to amend previously reported information: update information in narrative to "formally NSTEMI" from "formally STEMI".

Case Comment: Overall case causality: Probably Not Noting the patient's age, risk factors and underlying medical conditions, consider events to be more likely due to natural pathophysiology of infection and coronary atherosclerosis. Follow-up (11 March 2013): New information noted, but does not warrant change in previous assessment. Event remains probably not related to suspect drug. Follow-up: New information noted. Company causality updated to not related for both events.
Suspect drug has no immunosuppressive effect so it is unlikely for it to have a role on the pneumonia. The sudden death is also not related as patient has numerous comorbidities and risk factors which far outweigh the potential risk from the suspect drug. Follow-up: No change in previous company causality assessment. Follow-up: Newly added adverse event of renal insufficiency is not related as this was likely due to progression of preexistent conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	02-JAN-2013	Activated partial thromboplastin time	27 seconds	
2	02-JAN-2013	Band neutrophil count	0.18, X10**3/MCL	0.70 0
3	03-JAN-2013	Base excess	-2.7 mmol/L	
4	02-JAN-2013	Basophil count	0.03, X10**3/MCL	0.20 0.00
5	03-JAN-2013	Blood bicarbonate	19.5 mmol/L	28

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				20
6	03-JAN-2013	Blood bicarbonate	27.6 mmHg	45 35
7	02-JAN-2013	Blood cholesterol	126 mg/dl	200 120
8	02-JAN-2013	Blood creatine phosphokinase	81 IU/l	
9	17-DEC-2012	Blood creatinine	2.71 mg/dl	0.9 0.5
10	02-JAN-2013	Blood creatinine	2.1 mg/dl	0.9 0.5
11	17-DEC-2012	Blood erythropoietin	4.22 Mill/mcl,Unknown	
12	17-DEC-2012	Blood potassium	4.10 mmol/L	
13		Blood pressure measurement	186/73 mmHg	
14	02-JAN-2013	Blood triglycerides	95 mg/dl	200 55
15	02-JAN-2013	Blood urea	133 mg/dl	50 10
16	02-JAN-2013	Blood uric acid	11.3 mg/dl	6.8 2.5
17		Body temperature	37.2 Centigrade	
18	30-DEC-2012	Body temperature	38.2 Centigrade	
19	02-JAN-2013	C-reactive protein	3.7 mg/dl	0.6 0.1
20	30-DEC-2012	Chest X-ray	(Potential incipient infiltrate),Unknown	
21	30-DEC-2012	Chest X-ray	Cardiomegaly, chronic pulmonary vascular	
22	30-DEC-2012	Chest X-ray	Congestion, left basal increased streakingUnknown	
23	02-JAN-2013	Echocardiogram	Hypertension, and CHD,Unknown	
24	02-JAN-2013	Echocardiogram Hypertensive heart disease with normal left, Unknown	Hypertensive heart disease with normal left	
25	02-JAN-2013	Echocardiogram Insufficiency with severe pulmonary artery, Unknown	Insufficiency with severe pulmonaryarteryUnknown,	
26	02-JAN-2013	Echocardiogram Stenosis, mitral ring sclerosis, mild tricuspid, Unknown	Stenosis, mitral ring sclerosis, mild tricuspid,un	
27	02-JAN-2013	Echocardiogram Ventricular pump function, EF 57%,mild aortic, Unknown	Ventricular pump function, EF 57%mild aortic,unkn,	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
28	30-DEC-2012	Electrocardiogram (Loss of R-waves via the front wall,discrete ST),Unknown	Loss of R-waves via the front wall,discrete ST,Unk	
29	30-DEC-2012	Electrocardiogram (Depression V4-V6, T negative in II, III,aVF),unknown	Depression V4-V6, T negative in II, III,aVF Unknow	
30	30-DEC-2012	Electrocardiogram (VHF, frequency 121/min, right axis deviation,)Unknown	VHF, frequency 121/min, right axis deviation,Unkno	
31	31-DEC-2012	Electrocardiogram (VHF, 84/min, RT, incompl. RBBB, Av block I, T-neg)Unknown	VHF, 84/min, RT, incompl. RBBB, Av block I, T-neg	
32	31-DEC-2012	Electrocardiogram	In V5-V6.,Unknown	
33	02-JAN-2013	Eosinophil count	0.39,X10**3/MCL	0.45 0.00
34	17-DEC-2012	Haematocrit	36 %	
35	17-DEC-2012	Haemoglobin	12.20 g/dl	
36		Heart rate	121/min,Unknown	
37		Heart sounds	pure, arrhythmic,Unknown	
38	02-JAN-2013	High density lipoprotein	49 mg/dl	
39	17-DEC-2012	International normalised ratio	2.90 kA,Unknown	
40	04-JAN-2013	International normalised ratio	2.61,Unknown	3 2
41	02-JAN-2013	Low density lipoprotein	58 mg/dl	
42	02-JAN-2013	Lymphocyte count	1.02,X10**3/MCL	4.8 1.0
43	02-JAN-2013	Monocyte count	0.38,X10**3/MCL	0.8 0.0
44	02-JAN-2013	Neutrophil count	5.90 x 10 3 /mcl	7.7 1.8
45		Oxygen saturation	94 %	
46	03-JAN-2013	Oxygen saturation	95	
47	03-JAN-2013	PO2	70 mmHg	104 71
48		Physical examination	left basal quiet fine bubbly rattling,Unknown	
49		Physical examination	Without muscular guarding, pressure pain or	

Mfr. Control Number: 1595758

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
50		Physical examination	Upon examination by palpation. Renal bed wasUnkno,	
51		Physical examination Resistance. Liver and spleen were not enlarged Unknown	Resistance. Liver and spleen were not enlarged	
52		Physical examination Plantar on the left, right D1 medial dry necrosis Unknown	Plantar on the left, right D1 medial dry necrosis	
53		Physical examination Not painful to touch; had discrete lower leg Unknown	Not painful to touch; had discrete lower leg	
54		Physical examination Basal quiet fine bubble rattling. Heart tones,Unknown	Basal quiet fine bubble rattling. Heart tones	
55		Physical examination Pulmonary had vesicular respiratory sounds, left Unknown	Pulmonary had vesicular respiratory sounds, left	
56		Physical examination Edema on both sides, varicosis; had ulcer D1 Unknown	Edema on both sides, varicosis; had ulcer D1	
57		Physical examination	Were pure and arrhythmic. Abdomenwas,unjknown	
58	02-JAN-2013	Physical examination	5.90,X10**3/MCL	
59	17-DEC-2012	Platelet count	201 Tsd/mcl,Unknown	
60	02-JAN-2013	Platelet count	195,X10**3/MCL	
61	17-DEC-2012	Prothrombin time	23 %	
62	02-JAN-2013	Prothrombin time	61 %	
63	04-JAN-2013	Prothrombin time	35 %	
64		Respiratory rate	27/min,Unknown	
65		Troponin T	Elevated,Unknown	
66	02-JAN-2013	Troponin T	384,PG/ML	
67	03-JAN-2013	pH body fluid	7.47,Unknown	7.44 7.37

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	32 iu/kg/week, Freq: 3 Week;Interval:1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	11-JUN-2012 / 26-DEC-2014; 929 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) FERRLECIT /00345601/ (ASCORBIC ACID, FERRIC SODIUM CITRATE, FERROUS SULFATE, NICOTINAMIDE, RIBOFLAVIN, THIAMINE MONONITRATE) ; Unknown

#7) PANTOZOL /01263204/ (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

#8) SIMVABETA (SIMVASTATIN) Tablet ; Unknown

#9) VOTUM /01635402/ (OLMESARTAN MEDOXOMIL) ; Unknown

#10) AMLODIPINE (AMLODIPINE) Tablet ; Unknown

#11) ASS (ACETYLSALICYLIC ACID) Tablet ; Unknown

#12) BISOPROLOL (BISOPROLOL) Tablet ; Unknown

#13) CITALOPRAM (CITALOPRAM) Tablet ; Unknown

#14) RAMIPRIL (RAMIPRIL) Tablet ; Unknown

#15) TORASEMID (TORASEMIDE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption ang tobacco usage were not reported. Medical history included hyperlipidemia, ischemic heart disease from 1999, peripheral arterial disease from 30-Dec-2012, diabetes mellitus from 1999, hypertension and atrial fibrillation. It also included thumb amputation on the left around 1963, coronary 3 vessel disease, percutaneous transluminal coronary angioplasty (PTCA) and stent in the anterior interventricular artery in 1999, permanent VHF, mitral valve insufficiency grade I and II with left atrial dilatation, hypertensive nephropathy which led to renal failure diagnosed in 29-Nov-2005. The patient had acute to chronic kidney failure in 2010 with known nephropathyand nephroangiosclerosis, intermittent haemodialysis treatment via Shaldon catheter on the right groin, diabetic polyneuropathy with cl. pressure marks DI and II on the left traumatic finger. The patient had no allergies, drug hypersensitivities, or history of drug dependence. The patient was self-sufficient, and with mobile Rollator. Successful direct stenting of a 90% without restenosis was done on 15-Aug-2008. It was also reported that the patient had no problems for the last 23 months. Past drug therapy included moxifloxazine (dose and route of administration not reported), taken by the patient up to 05-May-2010. The patient was previously treated with an erythropoiesisstimulating agent (ESA) Aranesp (darbepoetin; mean dose: 167 mcg/week, dose also reported as 177 ng/kg/week for the last three months, route of administration not reported; from 08-Dec-2005 until 07-Jul-2012) and experienced percutaneous transluminal coronary angioplasty (PTCA) - RCX 90% STENT in Aug 2008 and lung edema (myocardial ischemia) on 23-Oct-2008. The patient died on 28-Dec-2014. Cause of death was renal insufficiency. It was not reported if an autopsy was performed. The patient's risk factors included obesity (33.3), coronary heart disease, atrial fibrillation, hypertension, diabetes type 2 with no diabetes
Unknown to Ongoing	Relevant Med History	Coronary artery disease (Coronary artery disease);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetic polyneuropathy (Diabetic neuropathy);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History 1999	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Left atrial dilatation (Left atrial dilatation);
Unknown to Ongoing	Relevant Med History Grade I and II	Mitral valve insufficiency (Mitral valve incompetence);
Unknown to Ongoing	Relevant Med History	Nephroangiosclerosis (Nephroangiosclerosis);
Unknown to Ongoing	Relevant Med History	Nephropathy (Nephropathy);
Unknown to Ongoing	Relevant Med History 30-Dec-2012	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Ventricular failure (Ventricular failure);
Unknown	Relevant Med History 15-Aug-2008	Stent placement (Stent placement);
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
Unknown	Relevant Med History Myocardial ischemia. 23-Oct 2008	Lung edema (Pulmonary oedema);
Unknown	Relevant Med History	Myocardial ischemia (Myocardial ischaemia);
Unknown	Relevant Med History RCX 90% Stent. 5 Aug 2008	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
Unknown	Relevant Med History in 1999	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
Unknown	Relevant Med History On the left, around 1963.	Thumb amputation (Finger amputation);
Unknown	Relevant Med History Risk Factor	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History Risk Factor	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor-1999	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor	Heart failure NYHA class II (Cardiac failure chronic);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor-33.3	Obesity (Obesity);
08-DEC-2005 to 07-JUL-2012	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Lung edema (Pulmonary oedema)
Unknown	Past Drug Event	DARBEPOETIN ALFA (DARBEPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Percutaneous transluminal coronary angioplasty (Coronary angioplasty)
05-MAY-2010 to Unknown	Past Drug Event	MOXIFLOXACIN (MOXIFLOXACIN); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
Unknown	Relevant Med History	Walker user (Walking aid user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	GERMANY	22	FEB	1957	55 Years	Male	100.00 kg	28	MAR	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Peripheral arterial occlusive disease [Peripheral arterial occlusive disease]
Death [Death]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO II) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia. This serious report describes a case of
peripheral arterial occlusive disease.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 01-JAN-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) Freq: 1 Week: Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 15-NOV-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown
#2) ASS (ACETYLSALICYLIC ACID) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Dec-2009	Cancer (Neoplasm malignant)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1614917

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-FEB-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case from a physician (reference: Ge-097-0020) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency and batch number not reported) for renal anaemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta. On 27-Mar-2012, the patient was hospitalized. On 28-Mar-2012, the patient experienced peripheral arterial occlusive disease. As an intervention for the adverse event, the patient underwent stent percutaneous transluminal angioplasty (PTA) annulus fibrosis stent (AFS right). The patient was hospitalized until 29-Mar-2012. Action taken with epoetin zeta in response to the adverse event and outcome of the event of peripheral arterial occlusive disease were not reported. The reporter's causality assessment for the event of peripheral arterial occlusive disease in relation to epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): Dose, batch number, expiry date, and previous exposure to other biosimilars. 05-Feb-2014: Follow up information was received from the investigator. Follow up report was created to reflect additional information regarding patient details, medical history, concomitant medications, adverse events, and reporter's causality assessment. Death was added as adverse event. This case describes a 55-year-old male patient (weight: 100 kg and height: 175 cm) who received Retacrit (one in a week, batch number unknown) from 15-Nov-2011. Medical history included hyperlipidemia in 2007, peripheral arterial disease in 2008, diabetes mellitus in 2011, and cancer in Dec-2009. It was reported that the patient experienced lower leg thrombosis on 21-Nov-2008 during previous treatment with other erythropoietin-stimulating agent (ESA); however, it was also reported that the patient was not at any time exposed to any other ESA. Concomitant medications included ASS (total daily dose: 100, unit not reported) and Plavix (total daily dose: 75, unit not reported), routes of administration not reported for unknown indications. On 15-Nov-2011, the patient started treatment with epoetin zeta. The patient received the last dose prior to the adverse event on 08-Mar-2012. The event of peripheral arterial occlusive disease was also reported as PAVK and the patient had lower leg pain. Outcome of the event of peripheral arterial occlusive disease was reported as persistent/significant disability. On 01-Jan-2014, the patient died. Cause of death was unknown. It was not reported if an autopsy was performed. The reporter's causality assessment for the events of death and peripheral arterial occlusive disease in relation to Retacrit was not related. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: dosage administered, batch number and expiry date.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without further objective clinical event details, cardiovascular risk factors, medical history and concomitant medications. - N. Gonzales (02 Mar 2013) Follow-up (10 Feb 2014): Overall case causality: Probably not The event is more likely due to the patient's underlying peripheral arterial disease with contributory effects from his hyperlidemic profile and other pre-existing risk factors for vascular occlusion. - R. Jacot

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage and medical history were not reported. 05-Feb-2014: Follow up information was received from the investigator regarding medical history and patient's death. Medical history included hyperlipidemia in 2007, peripheral arterial disease in 2008, diabetes mellitus in 2011, and cancer in Dec-2009. It was reported that the patient experienced lower leg thrombosis on 21-Nov-2008 during previous treatment with other erythropoietin-stimulating agent (ESA); however, it was also reported that the patient was not at any time exposed to any other ESA. On 01-Jan-2014, the patient died. Cause of death was unknown. It was not reported if an autopsy was performed. Race/ethnicity: Other
Unknown to Ongoing	Relevant Med History 2011	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History 2007	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History 2008	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Thrombosis leg (Thrombosis); with other ESA during treatment on 21-

Mfr. Control Number: 1614917

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Nov-2008	
Unknown	Past Drug Event	ALL OTHER THERAPEUTIC PRODUCTS (ALL OTHER THERAPEUTIC PRODUCTS); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Thrombosis leg (Thrombosis)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	24	JUL	1920	92 Years	Female	69.00 kg	06	SEP	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Lack of efficacy [Drug ineffective]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?
☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CARDIOASPIRIN (ACETYLSALICYLIC ACID) ; Unknown
#2) FOLIDEX (FOLIC ACID) ; Unknown
#3) ZYLORIC (ALLOPURINOL) ; Unknown
#4) BISOPROLOL (BISOPROLOL) ; Unknown
#5) ROCALTROL (CALCITRIOL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
30-JUN-2009 to 28-OCT-2011	Past Drug Event	
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1617854

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-APR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1617854

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

This is a Hospira-Sponsored Post authorisation safety cohort observation (PASCO II) of Retacrit (epoetin zeta), from Italy, administered subcutaneously, for the treatment of renal anaemia. This serious report describes a case of lack of efficacy. This case from a physician (reference: It-087-0004) describes a 92-year-old female who received Retacrit (epoetin zeta; subcutaneous, dose, frequency and batch number not reported) for renal anaemia on an unknown date. Medical history includes ongoing hypertension and ongoing renal failute. Past drug therapy included Aranesp (30 mcg, route of administration not reported) as erythropoetin stimulating agent. The patient experienced lack of efficacy during treatment with Aranesp; as corrective action, therapy was switched to Retacrit. Concomitant medications included Cardioaspirin (dose not reported, 1 of 1 day); Folidex 400 (1 of 1 day), bisoprolol 1.25 (1 of 1 day), Zyloric 300 (1/2 of 1 day), and rocaltrol 0.25 (1 of 1 day) (units of measure and routes of administration not reported); all given for unknown indications. On an unknown date, the patient began therapy with epoetin zeta. On 24-Aug-2012, the patient was hospitalised. On 06-Sep-2012, the patient experienced lack of efficacy. It was also reported that the patient had colostomy with blood loss. In response to the adverse event, the patient was given blood transfusion. It was reported that the patient was hospitalised until 08-Apr-2012. The event of lack of efficacy ended on 25-Feb-2013. The subject completed the study but the investigator could not provide more information in the report because the patient did not return to visit after having completed the study and the patient chart was not available anymore.
The reporter's causality assessment for the event of lack of efficacy in relation to epoetin zeta was not related.

Follow-up (01Feb2019): new information reported from the site includes: subject medical history, therapy status (subject withdrawn from the study).

Follow-up (04Apr2019): new information reported from the site includes subject completed the study and was not withdrawn from the study as previously reported.

Case Comment: Overall case causality: Not related Noting the chronology of event and a reporter causality of not related, it is very likely that the patient's anemia is aggravated by the colostomy blood loss, and thus needed to be treated with blood transfusion. Eryhtropoietin would not really be sufficient to treat such condition, regardless of efficacy or potency.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
30-JUN-2009 to 28-OCT-2011	Past Drug Event	ARANESP (ARANESP); Drug Indication: Renal anaemia (Nephrogenic anaemia), Drug Reaction: Drug ineffective (Drug ineffective) Past drug therapy included Aranesp (30 mcg, route of administration not reported) as erythropoetin stimulating agent. The patient experienced lack of efficacy during treatment with Aranesp; as corrective action, therapy was switched to Retacrit.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	07	JUL	1942	70 Years	Female	94.00 kg	28	JUL	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplexy [Cerebrovascular accident]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of thromboembolic
events. This serious case from an investigator (ref: Ge-027-0024) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency, formulation, and batch number not reported) for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 3000, Freq: 1 Week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 22-JUL-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) BICANORM (SODIUM BICARBONATE) Tablet ; 08-DEC-2009 / Unknown
#2) DEKRISTOL (COLECALCIFEROL) Capsule ; Unknown
#3) EXFORGE HCT (AMLODIPINE BESILATE, HYDROCHLOROTHIAZI
#4) FOSRENOL (LANTHANUM CARBONATE) Tablet ; Unknown
#5) MARCUMAR (PHENPROCOUMON) Tablet ; Unknown
#6) TORASEMID HEXAL (TORASEMIDE) Tablet ; 22-SEP-2009 / Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1647075

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-MAY-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

renal anaemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced thromboembolic events. Action taken with epoetin zeta, treatment and outcome of the adverse event were not reported. The reporter's causality assessment for the event of thromboembolic events in relation to epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number, date of expiry, and previous exposure to other biosimilars. 27-May-2013: Follow-up information received from the investigator. Follow-up report created to reflect new information regarding patient details, medical history, concomitant medications, suspect drug, adverse event and reporter's causality assessment. Reported term of adverse event was changed to apoplexy (previously reported as thromboembolic events). Patient was a 70-year-old female (weight: 94 kg and height: 168 cm). Patient's date of birth and ethnic origin were reported. The patient had previous exposure to other biosimilar, Erypo (mean dose 4000; unit of measure and route of administration not reported) from 20-Nov-2006 until 22-Jul-2011. The patient did not experience any thromboembolic event during treatment. Risk factors included obesity and smoking until 1970. Relevant concurrent diseases included hypertension and atrial fibrillation. Concomitant medications included torasemid Hexal 200 mg tablet (50 mg also reported as 1/4-0-0-0, daily) for edema, Bicanorm entericcoated tablet (4 g, 1-1-1-1, daily) for acidosis, Exforge HCT 10mg/320mg/25mg film-coated tablet (dose reported as 10/320/25, 1-0-0-0, daily) for hypertension, Marcumar tablet (according to Quick/INR, daily, dose not reported) for atrial fibrillation on Jul 2011, pantoprazol (20 mg, daily), Dekristol 20000 I.E. capsules IfAp (20000 I.E., 1-0-0-0, every 14 days), allopurinol AbZ 300 mg tablet (0-0-1-0), and Fosrenol 750 mg chewable tablet (1-1-1-0), all for unknown indications; all routes of administration not reported. The patient started treatment with epoetin zeta (3000, 1/week) on 22-Jul-2011. From 28-Jul-2012 until 08-Aug-2012, the patient was hospitalised due to the adverse event apoplexy with left hemiparesis. Treatment for the adverse event included anticoagulation (unspecified). On 16-Aug-2012, the patient recovered from the adverse event. The reporter's causality assessment for the event of apoplexy in relation to epoetin zeta was not related. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: batch number and date of expiry.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without firm time line, specific details about the reported event, medical history, concomitant medications, and pertinent laboratory results if any. - N. Gonzales (27 March 2013) Follow-up (07 Jun 2013): New information noted. Causality changed to not related as the event is more likely due to natural pathophysiology of the reported condition given the preexistent risk factors. - N. Gonzales (07 Jun 2013)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) EXFORGE HCT (AMLODIPINE BESILATE, HYDROCHLOROTHIAZIDE, VALSARTAN) Tablet ; 24-JUN-2010 / Unknown

#7) ALLOPURINOL (ALLOPURINOL) Tablet ; Unknown

#8) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 29-APR-2013 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage, and medical history were not reported. 27-May-2013: Follow-up information received from the investigator. Follow-up report created to reflect new information regarding medical history. The patient had previous exposure to other biosimilar, Erypo (mean dose 4000) from 20-Nov-2006 until 22-Jul-2011. The patient did not experience any thromboembolic event during treatment. Risk factors included obesity and smoking until 1970. Relevant concurrent diseases included hypertension and atrial fibrillation. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Obesity (Obesity);
Unknown	Relevant Med History Stop date: 1970	Ex-smoker (Ex-tobacco user);

Mfr. Control Number: 1647075

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event	ERYPO (ERYPO /00928301/); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	22	JUN	1934	78 Years	Male	95.30 kg	15	AUG	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: This is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). This report from Germany describes a case of NSTEMI. This serious case from
an investigator (reference: Ge-046-0010) describes a 78-year-old male patient (dry weight: 95.3 kg and height: 164 cm) who received Retacrit (epoetin zeta, subcutaneous, 3 times a week, batch number: 2E267F2; dose not reported) for renal

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2E267F2; Exp.Dt. 01-AUG-2014}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, Freq: 3 Week: Interval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 08-FEB-2012 / 11-AUG-2012

19. THERAPY DURATION
#1) 186 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS (ACETYLSALICYLIC ACID) ; 11-FEB-2010 / Unknown
#2) CALCET /00637401/ (CALCIUM CARBONATE, CALCIUM GLUCONATE
#3) DEKRISTOL (COLECALCIFEROL) ; 07-APR-2011 / Unknown
#4) FERMED /00023550/ (SACCHARATED IRON OXIDE) ; 11-JAN-2012 / Unknown
#5) LIMPTAR N (QUININE SULFATE) ; 23-APR-2012 / Unknown
#6) NOVORAPID (INSULIN ASPART) Solution for injection in pre-fille

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1837497

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-AUG-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

anaemia from 08-Feb-2012 until 11-Aug-2012. Medical history included hemodialysis, obesity with BMI of 35.3, significant and short term weight changes due to fluid retention/excretion on 17-Dec-2002, ischemic heart disease, and diabetes mellitus. The patient had no history of exposure to any other erythropoietin-stimulating agent. Concomitant medications were not reported. From 08-Feb-2012 until 11-Aug-2012, the patient received treatment with epoetin zeta. The patient was hospitalised on 13-Aug-2012. On 15-Aug-2012, the patient experienced NSTEMI. Treatment for the adverse event included PTCA with stenting of a coronary artery. Action taken with suspect drug was not reported. Outcome of the event of NSTEMI was recovered on 15-Aug-2012. On 23-Aug-2012, the patient was discharged from the hospital. The reporter's causality assessment for the event of NSTEMI in relation to the study medication epoetin zeta was not related.
The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dose administered. 21-Aug-2013: Follow up information received from the investigator. Follow-up report created to reflect new information regarding suspect drug and concomitant medications. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product epoetin zeta: dose administered. Dose of epoetin zeta was 3000 IE. Concomitant medications included ASS (100 mg, 0-1-0), bisoprolol (2.5 mg, 1-0-0), ramipril (10 mg, 1-0-0), amlodipin (10 mg, 1-0-1), torasemid (200 mg, 1/2-1/2-0), Calcet (950 mg, 1-1-1), Dekristol (20000 IE, route of administration not reported), MCP (4 mg/ml drops, if needed), Limptar N (1-0-0; dose not reported), Fermed (100 mg, 1x/month), doxazosin (4 mg, 1-0-0), Renavit (1-0-0; dose not reported), moxonidin (0.2 mg, 1-1-0-1), omeprazol (40 mg, 1-0-0), routes of administration not reported; Novorapid penfill and Protaphane penfill (doses and routes of administration not reported); all given for unknown indications. There was no action taken with the suspect drug in response to the event.

Case Comment: Overall case causality: Not related Patient had multiple preexisting risk factors for myocardial infection. - N. Gonzales (09 Aug 2013) Follow-up: No change in previous assessment. - N. Gonzales (29 Aug 2013)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) CALCET /00637401/ (CALCIUM CARBONATE, CALCIUM GLUCONATE, CALCIUM LACTATE, ERGOCALCIFEROL) ; 15-MAR-2012 / Unknown

#6) NOVORAPID (INSULIN ASPART) Solution for injection in pre-filled syringe ; 03-APR-2008 / Unknown

#7) PROTAPHANE (INSULIN HUMAN INJECTION, ISOPHANE) Solution for injection in pre-filled syringe ; 25-JUL-2009 / Unknown

#8) RENAVIT (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHENATE, FOLIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE MONONITRATE) ; 01-AUG-2012 / Unknown

#9) AMLODIPIN /00972401/ (AMLODIPINE) ; 11-FEB-2010 / Unknown

#10) BISOPROLOL (BISOPROLOL) ; 11-SEP-2012 / Unknown

#11) DOXAZOCIN (DOXAZOSIN MESILATE) ; 27-AUG-2011 / Unknown

#12) MCP /00041901/ (METOCLOPRAMIDE) ; 30-MAR-2010 / Unknown

#13) MOXONIDIN (MOXONIDINE) ; 19-FEB-2011 / Unknown

#14) OMEPRAZOL /00661201/ (OMEPRAZOLE) ; 09-MAR-2010 / Unknown

#15) RAMIPRIL (RAMIPRIL) ; 27-JAN-2009 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included hemodialysis, obesity with BMI of 35.3, significant and short term weight changes due to fluid retention/excretion on 17-Dec-2002, ischemic heart disease, and diabetes mellitus. The patient had no history of exposure to any other erythropoietin-stimulating agent. Race/Ethnicity: Caucasian

Mfr. Control Number: 1837497

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History BMI: 35.3	Obesity (Obesity);
Unknown	Relevant Med History 17-Dec-2002	Weight fluctuation (Weight fluctuation);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	22	SEP	1938	74 Years	Female	57.00 kg	27	FEB	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplex due to thrombose [Cerebrovascular accident]
Apoplex due to thrombose [Thrombosis]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany administered subcutaneously for the treatment of renal anaemia. This report from Germany describes a case of
apoplex due to thrombose.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IU, Freq: 1 Week; Interval:2

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Nephritis (Nephritis)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 26-JUN-2012 / 20-FEB-2013

19. THERAPY DURATION
#1) 240 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACTONEL (RISEDRONATE SODIUM) ; Unknown
#2) L-THYROXINE /00068001/ (LEVOTHYROXINE) ; Unknown
#3) MYFORTIC (MYCOPHENOLATE SODIUM) ; Unknown
#4) VIGANTOLETTEN (COLECALCIFEROL) ; Unknown
#5) AMIODARONE (AMIODARONE) ; Unknown
#6) DURADIURET (HYDROCHLOROTHIAZIDE, TRIAMTERENE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History from Nov-2003	Baker's cyst (Synovial cyst)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1857083

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-SEP-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This serious case from a physician (reference: Ge-151-0001) describes a 74-year-old female patient (weight: 57 kg and height: 165 cm) who received Retacrit (epoetin zeta; subcutaneous, once a week, and batch number unknown; dose, and formulation not reported) for nephritis from 26-Jun-2012 until 20-Feb-2013. Medical history included hypertension, chronic gastrointestinal disease from 2003; ostheopathy from Dec-2003, urinary tract infection from Nov-2003, baker cyst left knee from Nov-2003, and glaucoma both sides from Aug-2005 to 18-Feb-2013. It was also reported that the patient was exposed to other erythropoetin-stimulating agent (ESA, uspecified) and did not experience any thromboembolic event during treatment with other ESA. Past medications included Mircera (14.6), Silapo (10.2), and Neorecormon (11.0; units of measurement and routes of administration not reported), all given for unknown indications. Concomitant medications were not reported. On 26-Jun-2012, the patient started treatment with Retacrit. On 18-Feb-2013, the patient had surgery for glaucoma, 14 days without any significant symptoms. On 20-Feb-2013, therapy with Retacrit ended. On 27-Feb-2013, the patient complained of strong dizziness and problems with walking. On the same day, the patient was diagnosed with apoplex due to thrombose. The patient was admitted to the hospital on 01-Mar-2013. Treatment for the adverse event included theological liquid treatment (intravenous), oral anticoagulants Marcumar (dose not reported), antihypertensive, and diuretic medication, unspecified. Action taken with the suspect drug was not applicable. On 18-Mar-2013, the patient recovered from the adverse event and was discharged in the hospital. The reporter's causality assessment for the event of apoplex due to thrombose in relation to Retacrit was possible. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered. 30-Aug-2013: Additional information was received from the same reporter. Follow up report was created to reflect new information regarding suspect drug. The dose and frequency of epoetin zeta was reported as 6000 IE/2 weeks. 06-Sep-2013: English translation of the German discharge letter was received. Follow up report was created to reflect new information regarding medical history, laboratory results, and concomitant medications. Medical history included a suspected cerebral infarction, lacunar brain stem infarction with gait ataxia, dizziness, giddiness, progressive subcortical vascular encephalopathy, persistent atrial fibrillation, hyponatraemia, vitamin B12 deficiency, stage 2 chronic kidney disease, and status post kidney transplant in 2003. Concomitant medications included amiodarone 200 (1-0-0), ramipril 5 mg (1-0-0), metoprolol 95 (1-0-1), felodipine (1-0-0), duradiuret, furosemide, Actonel 35 mg (1x/week), Myfortic 360 mg (1-0-1), L-Thyroxine 125 (1-0-0), Vigantoletten 1000 IU (1-0-0); doses and routes of administration were not reported and all were given as premedications. The patient also had a long term (concurrent) therapy with Marcumar (dose and route of administration not reported) in personal anamnesis which was suspended at the time of admission due to eye surgery. Instead the patient was taking a daily heparin injection (dose and route of administration not reported). On 18-Feb-2013, the patient had a glaucoma surgery of the left eye. On 01-Mar-2013, the patient was initially admitted to the stroke unit. Continuous monitoring of vital parameters took place as well as regular monitoring of neurological, internal and psychological findings. These showed that the patient was stable, although the gait instability continued and showed only slow tendency to improve. In addition, the patient was also impaired from vision disturbances after the eye surgery. Upon neurological examination on an unknown date, the following information was noted; vigilance was alert, orientation was clearly oriented, no meningism; normal cranial nerve findings, no paralyses, proprioceptive reflex was reduced in the legs; no pathological reflexes, sensitivity noted a pallhypaesthesia in the feet, normal extrapyramidal symptoms, and coordination showed significant gait instability with a tendency to fall backwards and uncertain tendency to point left. Regular follow-up of neurological status showed gradual improvement of gait insecurity with other findings ongoing and persistent. Internal examination findings showed pretibial oedema on the right, heart rate rhythmic, cor showed pure heart tones, rhythmic; pulmo showed vesicular respiratory sounds with no crackles, the abdomen was soft with no pain on palpitation and peristaltic sounds were positive. Psychopathological findings showed that the patient was fully oriented, responsive; memory appears normal, friendly, and no evidence of psychotic symptoms. Both internal examination and psychopathological results indicated no indicatory abnormalities. Follow-up examinations indicated no significant changes. On 01-Mar-2013, at 20:46, creatinine was 1.85 mg/dl (reference value: 0.4-0.9 mg/dl), thromboplastin time was 112 % (reference value: 70-130 %), INR (I) was 0.94 (reference value 0.8-1.2, unit of measurement not reported), and aPTT was 24 sec (reference value: 25-35 sec). On the same day, cranial CT, non contrast showed a bifrontoparietal extension of the cerebral groove extending slightly beyond the range normal for the age as well as associated hypodense periventricular margins bilaterally and in the region of the white matter. Old lacunar changes interspersed here on both sides in the white matter, overall tending on the left side close to the anterior horn of the lateral ventricle and in the area of the external capsule. Similarly, smaller old lacunae also on the right side in the white matter section. In addition, cerebellar infarction peripheral paramedical on the right with a size of approx. 10 x 8 mm. No evidence of newly demarcated stroke areas. No intracranial haemorrhage. Basal vasoscleroses both in carotid siphon and in the basal area of the vertebral arteries that are still captured in the image. No evidence of CSF circulatory dysfunction in the midline structures. Frontoparietal calcification of the falx without disease status. Calcification of basal ganglia symmetrically on both sides and slight left-sided in terms of the density of calcification in the context of Fahr’s disease, without disease status. No evidence of masses. Paranasal sinuses, petrosal and mastoid cells aerated regularly and freely, symmetrically on both sides. Inner auditory canals normal size and appearance symmetrically on both sides. The CCT revealed an image of a cerebral microangiopathy and suspected infarction demarcation in the right cerebellum. On 02-Mar-2013, at 10:24, creatinine was 1.80 mg/dl, thromboplastin time was 102 %, INR (I) was 1.00, and aPTT was 32 sec. On 03-Mar-2013, neurosonological findings were normal with no evidence of higher grade stenosis or occlusions of the cranial arteries. On the same day, Doppler duplex examination was normal and showed no microangiopathy. On 05-Mar-2013, MEP for ant. tibia and EEG were normal. On 07-Mar-2013, electrophysiology showed no evidence of a gait disturbance and a normal electronystagmography (EOG). Gait assessment was normal. On 08-Mar-2013, tibial SEP was unavailable for both sides. On 11-Mar-2013, cranial MR, adult, infarction program, and non contrast showed inner

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

and outer CSF space extended normally for age sometimes extensively confluent signal enhancement in the white matter represented in the T2-w by vascular distribution, without evidence of new infarction event in the diffusion imaging. Lacunar substance defect in the basal ganglia region on the left and right cerebellar area, morphologically also predominantly corresponding to a vascular genesis. Extensive signal depressions on both sides in the basal ganglia region in the swi sequence, predominantly corresponding to regressive basal ganglia calcification. The mid-grade pronounced cerebral microangiopathy was also confirmed in a cranial MRI. Assessment showed no evidence of a new infarction event, pronounced vascular lesions on both sides, and regressive basal ganglia calcification. On 12-Mar-2013, FAEP and masseter reflex were normal. On the same day, blink reflex showed diffuse pontine lesions consistent with findings and tibial SEP showing the right as not available and left normal. Neurographic analysis showed no evidence of a polyneuropathy on an unknown date. On 13-Mar-2013, at 10:11, thromboplastin time was 23 % and INR (I) was 2.90. On 14-Mar-2013, blink reflex showed pontine lesions possibly on the right and left and potentially on the left. On 15-Mar-2013, at 10:54, thromboplastin time was 25 % and INR (I) was 2.70. As treatment, a rheological infusion and resume of the anticoagulation with Marcumar was done. Furthermore, the anti-hypertension and diuretic medication was modified. The patient also received intensive sensory motor exercise therapy and ergotherapy. Although there was a tendency toward improvement with the persistent deficit, a rehabilitation treatment was recommended to attain the fasted improvement of the deficit.

Case Comment: Overall case causality: Possible Suspect drug can theoretically lead to thromboembolic events based on mechanism of action, but consider also contibutory effects of patient's age and cardiovascular risk factors such as hypertension. - N. Gonzales (23 Aug 2013) Follow-up: No change in previous assessment. - N. Gonzales (07 Sep 2013) Follow-up: New information noted. Although patient already had a previous history of infarction, any possible contributory effects from the suspect drug cannot be totally ruled out. Causation remains possible. - N. Gonzales (15 Sep 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-MAR-2013	Activated partial thromboplastin time	24 seconds	35 25
2	02-MAR-2013	Activated partial thromboplastin time	32 seconds	35 25
3	01-MAR-2013	Blood creatinine	1.85 mg/dl	0.9 0.4
4	02-MAR-2013	Blood creatinine	1.80 mg/dl	0.9 0.4
5	01-MAR-2013	Blood thromboplastin	112 %	130 70
6	02-MAR-2013	Blood thromboplastin	102 %	130 70
7	13-MAR-2013	Blood thromboplastin	23 %	130 70
8	15-MAR-2013	Blood thromboplastin	25 %	130 70
9	01-MAR-2013	Computerised tomogram head	In the right cerebellum,Unknown	
10	01-MAR-2013	Computerised tomogram head	Suspected infarction demarcation,Unknown	
11	01-MAR-2013	Computerised tomogram head	Cerebral microangiopathy,Unknown	
12	12-MAR-2013	Corneal reflex decreased	Diffuse pontine lesions, Unknown	
13	14-MAR-2013	Corneal reflex decreased	Pontine lesions possibly on the right and left, U	
14	05-MAR-2013	Diagnostic procedure	Normal, Unknown	
15	12-MAR-2013	Diagnostic procedure	Normal, Unknown	
16	05-MAR-2013	Electroencephalogram	Normal, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
17		Electroneurography	No polyneuropathy, Unknown	
18	07-MAR-2013	Electronystagmogram	Normal, Unknown	
19	01-MAR-2013	International normalised ratio	0.94, Unknown	1.2 0.8
20	02-MAR-2013	International normalised ratio	1.00, Unknown	1.2 0.8
21	13-MAR-2013	International normalised ratio	2.90, Unknown	1.2 0.8
22	15-MAR-2013	International normalised ratio	2.70, Unknown	1.2 0.8
23	11-MAR-2013	Magnetic resonance imaging brain	Regressive basal ganglia calcification, Unknown	
24	11-MAR-2013	Magnetic resonance imaging brain	Pronounced vascular lesions on both sides, Unknown	
25	11-MAR-2013	Magnetic resonance imaging brain	No evidence of a new infarction event, Unknown	
26		Neurological examination	Uncertain tendency to point left, Unknown	
27		Neurological examination	No abnormalities, Unknown	
28		Neurological examination	Tendency to fall backwards, Unknown	
29		Neurological examination	Significant gait instability, Unknown	
30	07-MAR-2013	Neurological examination	No evidence of a gait disturbance, Unknown	
31		Physical examination	No abnormalities, Unknown	
32	12-MAR-2013	Reflex test normal	Normal, Unknown	
33	08-MAR-2013	Somatosensory evoked potentials	Unavailable for both sides, Unknown	
34	12-MAR-2013	Somatosensory evoked potentials	Right not available and left normal, Unknown	
35	03-MAR-2013	Ultrasound Doppler	No microangiopathy, Unknown	

13. Relevant Tests

Blink relfex: Pontine lesions possibly on the right and left, Unknbown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) FELODIPINE (FELODIPINE) ; Unknown

#8) FUROSEMIDE (FUROSEMIDE) ; Unknown

#9) METOPROLOL (METOPROLOL) ; Unknown

Mfr. Control Number: 1857083

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#10) RAMIPRIL (RAMIPRIL) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. Medical history included hypertension, chronic gastrointestinal disease from 2003; ostheopathy from Dec-2003, urinary tract infection from Nov-2003, baker cyst left knee from Nov-2003, and glaucoma both sides from Aug-2005 to 18-Feb-2013. It was also reported that the patient was exposed to other erythropoetin-stimulating agent (ESA, uspecified) and did not experience any thromboembolic event during treatment with other ESA. Past medications included Mircera (14.6), Silapo (10.2), and Neorecormon (11.0; units of measurement and routes of administration not reported), all given for unknown indications. Race/Ethnicity: Caucasian. 06-Sep-2013: Additional information was received from the same reporter. Follow up report was created to reflect new information regarding medical history. Medical history included a suspected cerebral infarction, lacunar brain stem infarction with gait ataxia, dizziness, giddiness, progressive subcortical vascular encephalopathy, persistent atrial fibrillation, hyponatraemia, vitamin B12 deficiency, stage 2 chronic kidney disease, and status post kidney transplant in 2003.
Unknown to Ongoing	Relevant Med History from 2003	Gastrointestinal disorder (Gastrointestinal disorder);
Unknown to Ongoing	Relevant Med History from Aug-2005 to 18-Feb-2013	Glaucoma both eyes (Glaucoma);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History from Dec-2003	Bone disorder (Bone disorder);
Unknown to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History from Nov-2003	Urinary tract infection (Urinary tract infection);
Unknown to Ongoing	Relevant Med History	Vitamin B12 deficiency (Vitamin B12 deficiency);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Brain stem infarction (Brain stem infarction);
Unknown	Relevant Med History	Cerebral infarction (Cerebral infarction);
Unknown	Relevant Med History	Dizziness (Dizziness);
Unknown	Relevant Med History	Ataxic gait (Ataxia);
Unknown	Relevant Med History	Giddiness (Dizziness);
Unknown	Relevant Med History	Glaucoma surgery (Glaucoma surgery);
Unknown	Relevant Med History	Hyponatraemia (Hyponatraemia);
Unknown	Relevant Med History in 2003	Kidney transplant (Renal transplant);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Subcortical vascular encephalopathy (Vascular encephalopathy);
Unknown	Past Drug Event	HEPARIN (HEPARIN); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
Unknown	Past Drug Event	MARCUMAR (MARCUMAR); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
13-DEC-2007 to 10-MAY-2012	Past Drug Event	MIRCERA (MIRCERA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
06-JUN-2005 to 13-DEC-2007	Past Drug Event	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
10-MAY-2012 to 19-JUN-2012	Past Drug Event	SILAPO (SILAPO); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	SEP	1938	74 Years	Female	63.40 kg	11	SEP	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiac Infarction [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of cardiac infarction.
This serious case from a physician (ref: Ge-046-0005) describes a 74-year-old female patient (weight: 63.4 kg; height: 163 cm) who received Retacrit (epoetin zeta; intravenous, twice a week; batch number unknown; dose not reported) for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) Freq: 2 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) Renal Anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History 06-May-2009	() Hyperlipidemia (Hyperlipidaemia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1915772

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-SEP-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1915772

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

renal anemia on an unknown date. Medical history included hypertension since 18-Dec-2007, hyperlipidemia since 06-May-2009, and peripheral arterial disease since 12-Jun-2009. The patient had no history of smoking and was not, at any time, exposed to any other erythropoetin-stimulatin agent (ESA). Concomitant medications were not reported. On an unknown date, the patient started treatment with epoetin zeta. Last dose prior to the adverse event was administered on 09-Sep-2013. On 11-Sep-2013, the patient experienced cardiac infarction described as non-ST segment elevation myocardial infarction (NSTEMI). It was reported that the patient was admitted to the hospital on the same day of 11-Sep-2013 because of this adverse event. It was reported that no coronary intervention was performed. Action taken with epoetin zeta was not reported. On an unknown date, the patient recovered from the event of cardiac infarction and was discharged from the hospital on 17-Sep-2013. The reporter's causality assessment of the event of cardiac infarction in relation to epoetin zeta was not related. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered.

Case Comment: Overall case causality: Not related Noting the presence of multiple cardiac risk factors in the medical history, consider the event to be more likely due to natural pathophysiology of coronary atherosclerosis. - N. Gonzales (23 Sep 2013)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. Medical history included hypertension since 18-Dec-2007, hyperlipidemia since 06-May-2009, and peripheral arterial disease since 12-Jun-2009. The patient had no history of smoking and was not, at any time, exposed to any other erythropoetin-stimulatin agent (ESA). Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History 18-Dec-2007	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History 12-Jun-2009	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	03	MAY	1936	77 Years	Male	90.50 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of NSTEMI. This
serious case from a physician (ref: Ge-048-0014) describing a case of a 77-year-old male patient (weight 90.5 kg; height 176 cm)who received Retacrit (epoetin zeta; subcutaneous, once a week; batch number not available; dose not

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IE, Freq: 1 Week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 18-JUN-2012 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Triple vessel disease (Coronary artery disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1940657

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-JUN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

reported) for renal anaemia since 18-Jun-2012. The patient had no history of smoking. Medical history included hypertension since 1980, chronic gastrointestinal disease described as collagenic colitis since 1995, ischemic heart disease since 2000, atrial fibrillation from Jan-2006 until Jan-2009, diabetes mellitus since 2006, hyperlipoproteinemia and hyperlipidemia before 2008, and peripheral arterial disease since 2008. The patient was not, at any time, exposed to any other erythropoetin-stimulating agent (ESA). Concomitant medications were not reported. On 18-Jun-2012, the patient received first dose of epoetin zeta. The patient received the last dose of epoetin zeta prior to the adverse event on 09-Sep-2013. On 13-Sep-2013, the patient was hospitalized due to chest pain. On an unknown date, the patient experienced non ST segment elevation myocardial infarction (NSTEMI). On 16-Sep-2013, coronary angiography was performed which revealed 99% stenosis at the right posterior lateral segment (RPLS) and coronary three vessel artery disease. Treatment for the adverse event included medical and interventional treatment. On an unknown date, percutaneous transluminal coronary angioplasty (PTCA) and drug-eluting (DE) stent implantation were performed. Action taken with epoetin zeta was not reported. The patient recovered from the adverse event on an unknown date. The patient was discharged from the hospital on 24-Sep-2013. The reporter's causality assessment of the event of NSTEMI in relation to epoetin zeta was not related. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered. 18-Oct-2013: English translation of the discharge letter from the physician was received. Follow up report was created to reflect additional information regarding the patient's medical history, adverse event, and laboratory and diagnostic tests. The patient's diabetes mellitus was described as type 2 currently dietary adjusted and hypertension was described as essential arterial hypertension. The patient had a history of ex-nicotine abuse. Other medical history of the patient included; 3 vessel coronary artery disease described as coronary 1-vessel disease MLTR diagonalis 1 - closure/recanalization attempt in 2003; history of N.Z tachyarrythmia absoluta in Jan-2004; serious mixed sleep apnea syndrome first diagnosed in January 2011 (no therapy because of masked gastrointestinal intolerance); Z.n pneumonia left in Mar-2011; hyperuricemia with gout of both feet in Apr-2011; chronic nephropathy III also reported as chronic renal failure STSD III with comp. a hypertensive vascular injury with renal anemia; benign prostatic hyperplasia, atrophic gastritis, known multifactorial anemia with vitamin B12 deficiency and renal insufficiency; polysegmental bony narrowing of the spinal canal and the neural foramina from L3/4 caudally; and previous cover plate compression fracture L2 and break of the cover plate also at L1 with appropriate reparation spondylophytes; secondary hyperparathyroidism; metabolic acidosis; infrarenal abdominal aortic aneurysm, dia. 2.73 cm in Aug-2013; and Budenofalk therapy. On 13-Sep-2013, the patient was admitted as inpatient at the Intensive Care Unit. According to the anamnesis of the patient, it was known that the patient was admitted for angina pectoris symptoms which had suddenly occurred during sitting. The patient also experienced thoracic discomfort. Initially, there was a visit to the emergency practice. An atrial flutter and atrial fibrillation was seen during the course which is why the patient needed to be transferred to another hospital. This resulted in ST segment depression in the posterolateral ECG and a laborohemic troponin elevation resulting in the admission to the ICU. Physical examination revealed that the patient was in good AZ and good EZ; head and neck was inconspicuous; sonorous percussion and VAG over the lungs; pure HT; rhythmic RF; abdomen soft; no defensive tension; no resistance; no DS; renal bed free; no knocking pain in the spine; and neurological orienting grossly unremarkable. ECG revelaed sinus rhythm, HF 80/min, ULT, LAH, ST segment depression V3-V6. It was also reported that within the course, there was SR, HF 49/min, OLT, and LAH. Therapy with ASS, clopidogrel, and heparin (doses and routes of administration not reported) was performed. The patient did not cite any other thoracic complaints; however, laboratory chemistry showed troponin increase. An intermittent provision with nitroprusside syringe pump (dose and route of administration not reported) during the course at increased RR values was converted to RR medication. On 16-Sep-2013, the patient was discharged from the hospital and the patient was transferred to another hospital for coronary angiography at an existing renal insufficiency. The patient was informed to drink enough liquids so that the creatinine values were last at 1.25 mg/L. On 16-Sep-2013, the patient was admitted to another hospital for coronary angiography. Physical examination on admission revealed that the patient was chronically reduced AZ and good EZ. No upper vena cava. Heart sounds with a slight systolic murmur in the second ICR right. Lungs on both sides with vesicular breathing sound. Abdomen soft, no herniation, no pressure pain, no peripheral edema. Inconspicuous peripheral pulse status and orienting neurological status. Also on 16-Sep-2013, at 10:15:00, APTT was 36 sec (normal range: 26 - 40), troponin Ths was 78 g/ml (normal value -100), potassium was 4.6 mmol/L (normal range: 3.5 - 5.1), sodium was 135 mmol/L (normal range: 135 - 145), creatinine was 1.79 mg/dl (normal range: 0.6 - 1.3), GOT 37 degrees Celsius IFCC with pyridoxal ph was 31 U/L (normal range: 10 - 51), AP 37 degrees Celsius was 73 U/L (normal value: -98), LDH 37 degrees Celsius was 198 U/L (normal value: -266), CK 37 degrees Celsius was 113 U/L (normal value: -174), CK-MB 37 degrees Celsius was 16 U/L (normal value: -24), QUICK was 108% (normal value: 70-),leukocytes was 7.20/nl (normal range: 4.3 - 10.0), hemoglobin was 12.6 g/dl (normal range: 14.0 - 18.0), hematocrit was 0.366 l/l Quotient (normal range: 0.410 - 0.530), platelets was 223/nl (normal range: 150 - 350), GFR-estimate was 39 ml/min/1.73m^2 (normal range: 90 - 150), glucose was 108 mg/dl (normal range: 60 - 100), erythrocytes was 3.98/pl (normal range: 4.5 - 5.9), MCV was 92.0 fl (normal range: 80 - 96), MCH was 31.7 pg (normal range: 28 - 33), MCHC was 34.4 g/dl (normal range: 32 - 36), RDW was 41.1 fl (normal range: 35.1 - 43.9), INR was 0.95 (unit of measurement and normal value not reported), and TSH was 2.250 mU/L (normal range: 0.27 - 4.2). On the same day, at 15:15:00, troponin Ths was 91 pg/ml, potassium was 4.7 mmol/L, LDH 37 degrees Celsius was 180 U/L, CK 37 degrees Celsius was 112 U/L, and CK-MB 37 degrees Celsius was 13 U/L. Cardiac catheter report HZE 4195-13 also reported as coronary angiography for NSTEMI on 16-Sep-2013 was performed after presoaking. AOA was sys = 188, dia = 72, and M - 112 while resting (units of measurement and normal values not reported). LMVO was not performed due to renal failure. HST was WUR. On LAD, there was ostial 25-50% stenosis and diffuse vasosclerosis during the process. On RCX, there was 99% RPIS stenosis and 50 - 75% RCX stenosis. On RCA, there was 50% stenosis in the pars descendens. The RCXPCI

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

procedure used EBU 4.0 SH. There was trouble-free wire passage with BMW. PTCA with 2.0/15 mm Trek balloon to 16 bar, then implant of a 2.5/12 mm Xience Pro DES with 16 bar and good final result. Diagnosis of 3-vessel coronary disease with NSTEMI and successful RPLS PCI with 1x DES implantation was confirmed and 25-50% LAD and 50-75% RCS stenosis remained. The procedure also showed a progressive coronary heart disease. The post-interventional trial proved uneventful and the kidneys showed stable values under infusion therapy. On 17-Sep-2013, APTT was 37 sec, PCT quant. was 0.14 ng/ml (normal value: -0.5), troponin Ths was 113 pg/ml, potassium was 4.7 mmol/L, sodium was 134 mmol/L, creatinine was 1.80 mg/dl, urea was 58 mg/dl (normal value: -50), triglyceride was 202 ntg/dl (normal value: -200), HDL-cholesterol was 42 mg/dl (normal value: 35-), GOT 37 degrees Celsius IFCC with pyridoxal ph was 42 U/L, GPT 37 degrees Celsius IFCC with pyridoxal ph was 40 U/L (normal range: 10 - 50), Gamma-GT 37 degrees Celsius was 42 U/L (normal value: -66), AP 37 degrees Celsius was 75 U/L, LDH 37 degrees Celsius was 251 U/L, CK 37 degrees Celsius was 104 U/L, CK-MB 37 degrees Celsius was 21 U/L, ferritin was 290.1 ng/ml (normal range: 30 - 400), QUICK was 100%, leukocytes was 7.40/nl, hemoglobin was 12.2 g/dl, hematocrit was 0.355 l/l Quotient, platelets was 225/nl, cholesterol was 201 mg/dl (normal value: -200), LDL-cholesterol was 119 mg/dl (normal value: -155), C-reactive protein was 0.2 mg/dl (normal value: -0.5), GFR-estimate was 39 ml/min/1.73 m^2, erythrocytes was 3.87/pl, MCV was 91.7 fl, MCH was 31.5 pg, MCHC was 34.4 g/dl, RDW was 40.1 fl, and INR was 1.00 (unit of measurement not reported). On an unknown date, puncture pancreatic amylase was 25 U/L (normal range: 8 - 53). Also on an unknown date, rest ECG revealed bradycardic sinus rhythm, heart rate of 47/min, overtightened left type at left anterior hemiblock, hesitant R-progression, and no partial chamber end changes. It was reported that progress of ECG was status idem. On 18-Sep-2013, transthoracic echocardiography (TTE) was performed which revealed slightly detailed left atrium, other cardiac cavities normal size, normal values of the aorta ascendens, light concentric LV hypertrophy, and left inconspicuous ventricular resting function. Relaxation interference. No pericardial effusion. Aortic valve thickening, increased echo factor and with moderately limited separation. Mitral, tricuspid and pulmonary valve morphological and inconspicuous in motion. IAS morphological and inconspicuous in Doppler. Aortic stenosis II, after continuity equation, a calculated valve opening surface of about 1.4 cm^2 (P max 24 mmHg, P mean 12 mmHg). No significant aortic regurgitation. Otherwise unremarkable Doppler spectra to the other heart valves. A good systolic pump function without regional wall movement interferences was echocardiographically documented. The mobilization of the patient was free of problems and can be transferred back to his home hospital. The hospital requested for a continuation of the heart insuficiency medication and the dual antiplatelet therapy (unspecified; doses and routes of administration not reported). A subsequent medical action is meaningful and outpatient cardiology in connection with a regular echocardiographic follow-up of the aortic valve stenosis. The hospital also recommended clopidogrel for one year, ASA permanent heart failure medication and secondary prevention (doses and routes of administration not reported). On 19-Sep-2013, the patient was re-admitted to his home hospital after a coronary angiography. The patient had low grade deterioration of renal function after coronary angiography. Physical examination upon admission showed that the patient was in good general condition, moderately adiposely nourished, consciousness inconspicuous, spirit inconspicuous, movements inconspicuous, speech inconspicuous, skin inconspicuous with hematoma left lower abdomen (Clexane injections) and right groin (puncture from cardiac catheter), as well as age spots mostly on the back, no edemas, no distinctions on head and neck. Pulmonary examination showed vesicular respiratory sound, sonorous percussion, inconspicuous lung limitations. Heart sounds 2/6 end-diastolic noise rhythmic, abdomen soft, no break, diastasis recti, no resistance, kidney bearing inconspicuous, liver and spleen inconspicuous, auscultatory regular peristalsis in all four quadrants, free nerve exit points, pupils round, light responsive, coordination inconspicuous inconspicuous sensibility, grip strength inconspicuous, no vegetative signs. Right groin generally isolated hematoma. On ECG, there was sinus rhythm, normofrequent at 52/min, left to type overtightened left type, discrete ST segment elevation in V1, avr, discrete ST-segment depression in I, II, V5, V6. Duplex sonography of the pelvic and leg veins revealed no evidence of a right LVT and no indication of a false aneurysm. On 20-Sep-2013 nephrological consult confirmed a diagnosis of chronic renal insufficiency Stage III at Verd. a. vascular nephropathy, acute renal failure after coronary angiography, and a creatinine increase of 1.3 to 1.7 (unit of measurement not reported). The patient had no dyspnea, no orthopnea, no kidney pain, no hematuria observed, no dizziness, no edema, renal capsule is not painful to pulse regularly, bradycardiac 40/min. On the same day, long term blood pressure monitoring showed average blood pressure 150/76 mmHg, average HF 42/Min., obtained night setback (normal values not reported). During the day on average 150/77 mmHg, HF 42/Min., at night on average 148/72 mmHg, HF = 40/min., thus on average still 79% of the systole and 17% of diastole above the target limit. On 23-Sep-2013, laboratory data included leukocytes of 8030/mcl (normal range: 3500 - 9800), erythrocytes of 3.8/pl (normal range: 4.5 - 5.9), hemoglobin was 11.8 g/dl (normal range: 13.5 - 17.5), hematocrit 34.9% (normal range: 40 - 53), MCV was 92.3 fl (normal range: 80 - 96), MCH was 31.2 pg/Ery (normal range: 28 - 33), MCHC was 33.8 g/dl (normal range: 32 - 35), platelets was 252/nl (normal range: 140 - 360), GOT was 33 U/L (normal range: 10 - 59), GPT was 43 U/L (normal range: 10 - 50), sodium was 142 mmol/L (normal range: 135 - 145), potassium was 4.2 mmol/L (normal range: 3.5 - 5.1), calcium was 2.3 mmol/L (normal range: 2.0 - 2.6), urea was 67 mg/dl (normal value: less than 50), creatinine was 1.7 mg/dl (normal value: less than 1.2), CK was 105 U/L (normal value: less than 190), CK-MB was 13 U/L (normal value: less than 25), LDH was 195 U/L (normal value: less than 250), HbA1c (DCCT) was 5.6% (normal range: 4 - 6), HbA1c (FCC) was 37.7 mmol/mol Hb (normal range: 20 - 42), average glucose value was 114 mg/dl (normal range: 68 - 126), and glomerular filtration rate was 39.3 ml/min (normal value: greater than 68). A nephrological consult at a creatine increase was conducted. An increased liquid substitution and daily weighing was also recommended. Base on the initially viewed atrial fibrillation and atrial flutter, a long-term ECG was conducted and a continuous rather bradycardic sinus rhythm was documented. The physician waived an oral anti-coagulation at an only anamnestic atrial fibrillation despite an CHA2DS2-VASc score of 4, however, which should be initiated after completion of the dual platelet aggregation after the DES implantation or when documenting an atrial fibrillation in the planned LZ ECGs. On 24-Sep-2013, the patient was discharged from his home hospital. 04-Jun-2014: Additional information was received from the investigator. Follow up report was created to reflect additional information regarding the patient's medical history and suspect drug. The reporter was able to provide the following

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

information regarding the identification and traceability of the biosimilar product epoetin zeta: dosage administered and previous exposure of patient to other biosimilars. The patient did not have previous exposure to other biosimilar products. Dose of Retacrit was 2000 IE.

Case Comment: Overall case causality: Probably Not Although by mechanism of action, the increase in red blood cells by Epoetin can potentially contribute to the development of ischemia, patient has multiple cardiovascular risk factors in the medical history which have stronger association with the reported event. - N. Gonzales (10 Oct 2013) Follow-up: New information noted. Case remains probably not related to suspect drug. - N. Gonzales (28 Oct 2013) Follow-up (12 June 2014): New information noted, but does not warrant change in previous causality assessment. Causality entered on behalf of Dr. N. Gonzales by J.Fernando

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	16-SEP-2013	Activated partial thromboplastin time	36 seconds	40 26
2	17-SEP-2013	Activated partial thromboplastin time	37 seconds	40 26
3	17-SEP-2013	Alanine aminotransferase	40 IU/l	50 10
4	23-SEP-2013	Alanine aminotransferase	43 IU/l	50 10
5		Amylase	25 IU/l	53 8
6	16-SEP-2013	Angiocardiogram	99% stenosis at the RPLS, Unknown	
7	16-SEP-2013	Angiocardiogram	Coronary three vessel artery disease, Unknown	
8	16-SEP-2013	Aspartate aminotransferase	31 IU/l	51 10
9	17-SEP-2013	Aspartate aminotransferase	42 IU/l	51 10
10	23-SEP-2013	Aspartate aminotransferase	33 IU/l	59 10
11	16-SEP-2013	Blood alkaline phosphatase	73 IU/l	
12	17-SEP-2013	Blood alkaline phosphatase	75 IU/l	
13	23-SEP-2013	Blood calcium	2.3 mmol/l	2.6 2.0
14	17-SEP-2013	Blood cholesterol	201 mg/dl	
15	16-SEP-2013	Blood creatine phosphokinase	112 IU/l	
16	16-SEP-2013	Blood creatine phosphokinase	113 IU/l	
17	17-SEP-2013	Blood creatine phosphokinase	104 IU/l	
18	23-SEP-2013	Blood creatine phosphokinase	105 IU/l	
19	16-SEP-2013	Blood creatine phosphokinase MB	16 IU/l	
20	16-SEP-2013	Blood creatine phosphokinase MB	13 IU/l	
21	17-SEP-2013	Blood creatine phosphokinase MB	21 IU/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
22	23-SEP-2013	Blood creatine phosphokinase MB	13 IU/l	
23	16-SEP-2013	Blood creatinine	1.79 mg/dl	1.3 0.6
24	17-SEP-2013	Blood creatinine	1.80 mg/dl	1.3 0.6
25	20-SEP-2013	Blood creatinine	Increase of 1.3 to 1.7, Unknown	
26	23-SEP-2013	Blood creatinine	1.7 mg/dl	
27	16-SEP-2013	Blood glucose	108 mg/dl	100 60
28	23-SEP-2013	Blood glucose	114 mg/dl	126 68
29	16-SEP-2013	Blood lactate dehydrogenase	180 IU/l	
30	16-SEP-2013	Blood lactate dehydrogenase	198 IU/l	
31	17-SEP-2013	Blood lactate dehydrogenase	251 IU/l	
32	23-SEP-2013	Blood lactate dehydrogenase	195 IU/l	
33	16-SEP-2013	Blood potassium	4.6 mmol/l	5.1 3.5
34	16-SEP-2013	Blood potassium	4.7 mmol/l	5.1 3.5
35	17-SEP-2013	Blood potassium	4.7 mmol/l	5.1 3.5
36	23-SEP-2013	Blood potassium	4.2 mmol/l	5.1 3.5
37	16-SEP-2013	Blood pressure diastolic	72, Unknown	
38	20-SEP-2013	Blood pressure measurement	During the day, average BP of 150/77 mmHg	
39	20-SEP-2013	Blood pressure measurement	At night, average BP of 148/72 mmHg	
40	20-SEP-2013	Blood pressure measurement	Average BP of 150/76 mmHg	
41	16-SEP-2013	Blood pressure systolic	188, Unknown	
42	16-SEP-2013	Blood sodium	135 mmol/l	145 135
43	17-SEP-2013	Blood sodium	134 mmol/l	145 135
44	23-SEP-2013	Blood sodium	142 mmol/l	145 135
45	16-SEP-2013	Blood thyroid stimulating hormone	2.250, MU/L	4.2 0.27
46	17-SEP-2013	Blood triglycerides	202 ntg/dl, Unknown	
47	17-SEP-2013	Blood urea	58 mg/dl	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
48	23-SEP-2013	Blood urea	67 mg/dl	
49		Breath sounds	Vesicular, Unknown	
50	16-SEP-2013	Breath sounds	Lungs on both sides with vesicular breathing sound	
51	17-SEP-2013	C-reactive protein	0.2 mg/dl	
52	18-SEP-2013	Echocardiogram	Normal values of the aorta ascendens, Unknown	
53	18-SEP-2013	Echocardiogram	Slightly detailed left atrium, Unknown	
54	18-SEP-2013	Echocardiogram	No pericardial effusion, relaxation interference,	
55	18-SEP-2013	Echocardiogram	Increased echo factor, Unknown	
56	18-SEP-2013	Echocardiogram	1.4 cm^2 (P max 24 mmHg, P mean12 mmHg), Unknown	
57	18-SEP-2013	Echocardiogram	and inconspicuous in motion, Unknown	
58	18-SEP-2013	Echocardiogram	Aortic stenosis II, Unknown	
59	18-SEP-2013	Echocardiogram	Aortic valve thickening, Unknown	
60	18-SEP-2013	Echocardiogram	Calculated valve opening surface, Unknown	
61	18-SEP-2013	Echocardiogram	Good systolic pump function, Unknown	
62	18-SEP-2013	Echocardiogram	Left inconspicuous ventricular resting function, U	
63	18-SEP-2013	Echocardiogram	Light concentric LV hypertrophy, Unknown	
64	18-SEP-2013	Echocardiogram	Mitral, tricuspid, pulmonary valve morphological,	
65	18-SEP-2013	Echocardiogram	No significant aortic regurgitation, Unknown	
66	18-SEP-2013	Echocardiogram	Other cardiac cavities normal size, Unknown	
67	18-SEP-2013	Echocardiogram	With moderately limited separation, Unknown	
68	18-SEP-2013	Echocardiogram	Without regional wall movement interferences, Unkn	
69		Electrocardiogram	Continuous rather bradycardic sinusrhythm, Unknown	
70		Electrocardiogram	Discrete ST segment elevation in V1, avr, Unknown	
71		Electrocardiogram	Hesitant R-progression,	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			Unknown	
72		Electrocardiogram	No partial chamber end changes, Unknown	
73		Electrocardiogram	Overtightened left type left anterior hemiblock, U	
74		Electrocardiogram	Sinus rhythm,ULT,LAH,ST segmentdepression V3-V6	
75		Electrocardiogram	Bradycardic sinus rhythm, Unknown	
76		Electrocardiogram	Discrete ST segment depression in I,II, V5, V6, Un	
77		Electrocardiogram	Left to type overtightened left type, Unknown	
78		Electrocardiogram	Sinus rhythm, normofrequent at 52/min, Unknown	
79		Electrocardiogram	ST segment depression, Unknown	
80	17-SEP-2013	Gamma-glutamyltransferase	42 IU/l	
81	16-SEP-2013	Glomerular filtration rate	39 ml/min/1.73 m^2, Unknown	150 90
82	17-SEP-2013	Glomerular filtration rate	39 ml/min/1.73 m^2, Unknown	150 90
83	23-SEP-2013	Glomerular filtration rate	39.3 ml/min	
84	23-SEP-2013	Glycosylated haemoglobin	37.7 mmol/mol Hb, Unknown	42 20
85	23-SEP-2013	Glycosylated haemoglobin	5.6 %	6 4
86	16-SEP-2013	Haematocrit	0.366 l/l quotient, Unknown	0.530 0.410
87	17-SEP-2013	Haematocrit	0.355 l/l quotient, Unknown	0.530 0.410
88	23-SEP-2013	Haematocrit	34.9 %	53 40
89	16-SEP-2013	Haemoglobin	12.6 g/dl	18.0 14.0
90	17-SEP-2013	Haemoglobin	12.2 g/dl	18.0 14.0
91	23-SEP-2013	Haemoglobin	11.8 g/dl	17.5 13.5
92		Heart rate	49/min, Unknown	
93		Heart rate	80/min, Unknown	
94		Heart rate	47/min, Unknown	
95	20-SEP-2013	Heart rate	Average 42/min, Unknown	
96	20-SEP-2013	Heart rate	Average at night, 40/min, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
97	20-SEP-2013	Heart rate	Average during the day, 42/min, Unknown	
98	20-SEP-2013	Heart rate	40/min, Unknown	
99	16-SEP-2013	Heart sounds	Slight systolic murmur in the second ICR right, Un	
100	19-SEP-2013	Heart sounds	2/6 end-diastolic noise rhythmic, Unknown	
101	17-SEP-2013	High density lipoprotein	42 mg/dl	
102	16-SEP-2013	International normalised ratio	0.95, Unknown	
103	17-SEP-2013	International normalised ratio	1.00, Unknown	
104	17-SEP-2013	Low density lipoprotein	119 mg/dl	
105	16-SEP-2013	Mean arterial pressure	112, Unknown	
106	16-SEP-2013	Mean cell haemoglobin	31.7 pg	33 28
107	17-SEP-2013	Mean cell haemoglobin	31.5 pg	33 28
108	23-SEP-2013	Mean cell haemoglobin	31.7 pg/Ery, Unknown	33 28
109	16-SEP-2013	Mean cell haemoglobin concentration	34.4 g/dl	36 32
110	17-SEP-2013	Mean cell haemoglobin concentration	34.4 g/dl	36 32
111	23-SEP-2013	Mean cell haemoglobin concentration	33.8 g/dl	35 32
112	16-SEP-2013	Mean cell volume	92.0, FL	96 80
113	17-SEP-2013	Mean cell volume	91.7, FL	96 80
114	23-SEP-2013	Mean cell volume	92.3, FL	96 80
115		Neurological examination	Grossly unremarkable, Unknown	
116	16-SEP-2013	Neurological examination	Orienting, Unknown	
117		Physical examination	Sonorous percussion,VAG over lungs, Unknown	
118		Physical examination	Head and neck inconspicuous, Unknown	
119		Physical examination	Pure HT, rhythmic RF, abdomen soft, Unknown	
120		Physical examination	Renal bed free, no knocking pain in the spine, Unk	
121		Physical examination	No defensive tension, no	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			resistance,no DS, Unknown	
122	16-SEP-2013	Physical examination	Inconspicuous pulse status, Unknown	
123	16-SEP-2013	Physical examination	Chronically reduced AZ and good EZ, Unknown	
124	16-SEP-2013	Physical examination	No upper vena cava, abdomen soft, no herniation, U	
125	16-SEP-2013	Physical examination	No pressure pain, no peripheral edema, Unknown	
126	19-SEP-2013	Physical examination	Right groin generally isolated hematoma, Unknown	
127	19-SEP-2013	Physical examination	No distinctions on head and neck, Unknown	
128	19-SEP-2013	Physical examination	Light responsive coordination, Unknown	
129	19-SEP-2013	Physical examination	Kidney bearing inconspicuous, Unknown	
130	19-SEP-2013	Physical examination	Hematoma left lower abdomen and right groin, Unkno	
131	19-SEP-2013	Physical examination	Grip stregth inconspicuous, no vegetative signs, U	
132	19-SEP-2013	Physical examination	Good general condition, Unknown	
133	19-SEP-2013	Physical examination	Consciousness, spirit, and movements inconspicuous	
134	19-SEP-2013	Physical examination	Auscultatory regular peristalsis in 4quadrants, Un	
135	19-SEP-2013	Physical examination	Age spots mostly on the back, no edemas, Unknown	
136	19-SEP-2013	Physical examination	Moderately adiposely nourished, Unknown	
137	19-SEP-2013	Physical examination	Abdomen soft, no break, Unknown	
138	19-SEP-2013	Physical examination	Diastasis recti, no resistance, Unknown	
139	19-SEP-2013	Physical examination	Free nerve exit points, pupils rounds, Unknown	
140	19-SEP-2013	Physical examination	inconspicuous sensibility, Unknown	
141	19-SEP-2013	Physical examination	Liver and spleen inconspicuous, Unknown	
142	19-SEP-2013	Physical examination	Speech and skin inconspicuous, Unknown	
143	19-SEP-2013	Physical examination	Sonorous percussion,inconspicuous lung limitation,	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
144	20-SEP-2013	Physical examination	Renal capsule not painful to pulse regularly, Unkn	
145	20-SEP-2013	Physical examination	No dyspnea, no orthopnea, no kidney pain, Unknown	
146	20-SEP-2013	Physical examination	No hematuria, no dizziness, no edema, Unknown	
147	16-SEP-2013	Platelet count	223/nl, Unknown	350 150
148	17-SEP-2013	Platelet count	225/nl, Unknown	350 150
149	23-SEP-2013	Platelet count	252/nl, Unknown	360 140
150	17-SEP-2013	Procalcitonin	0.14 ng/ml	
151	16-SEP-2013	Prothrombin time	108 %	
152	17-SEP-2013	Prothrombin time	100 %	
153	16-SEP-2013	Red blood cell count	3.98/pl, Unknown	5.9 4.5
154	17-SEP-2013	Red blood cell count	3.87/pl, Unknown	5.9 4.5
155	23-SEP-2013	Red blood cell count	3.8/pl, Unknown	5.9 4.5
156	16-SEP-2013	Red cell distribution width	41.1, FL	43.9 35.1
157	17-SEP-2013	Red cell distribution width	40.1, FL	43.9 35.1
158		Renal function test	Stable values, Unknown	
159	17-SEP-2013	Serum ferritin	290.1 ng/ml	400 30
160		Troponin	Increase, Unknown	
161		Troponin	Elevation, Unknown	
162	16-SEP-2013	Troponin	91, PG/ML	
163	16-SEP-2013	Troponin	78, PG/ML	
164	17-SEP-2013	Troponin	113, PG/ML	
165		Ultrasound Doppler	No evidence of right LVT, Unknown	
166		Ultrasound Doppler	No indication of false aneurysm, Unknown	
167	18-SEP-2013	Ultrasound Doppler	IAS morphological and inconspicuous, Unknown	
168	18-SEP-2013	Ultrasound Doppler	Unremarkable spectra to other heart valves, Unknow	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
169	16-SEP-2013	White blood cell count	7.20/nl, Unknown	10.0 4.3
170	17-SEP-2013	White blood cell count	7.40/nl, Unknown	10.0 4.3
171	23-SEP-2013	White blood cell count	8030/mcl, Unknown	9800 3500

13. Relevant Tests

Breathing sounds (16-Sep-2013): Lungs on both sides with vesicular breathing sound, Unknown
ECG: Discrete ST segment depression in I,II, V5, V6, Unknown
ECG: Sinus rhythm,ULT,LAH,ST segmentdepression V3-V6, Unknown
Heart sounds(16-Sep-2013): Slight systolic murmur in the second ICR right, Unknown
Physical examination: Renal bed free, no knocking pain in the spine, Unknown
Pulmonary examination(19-Sep-2013): Sonorous percussion,inconspicuous lung limitation, Unknown
Physical examination(16-Sep-2013): No upper vena cava, abdomen soft, no herniation, Unknown
Physical examination (19-Sep-2013): Auscultatory regular peristalsis in 4quadrants, Unknown
Physical examination (19-Sep-2013): Consciousness, spirit, and movements inconspicuous, Unknown
Physical examination (19-Sep-2013): Grip stregth inconspicuous, no vegetative signs, Unknown
Physical examination (19-Sep-2013): Hematoma left lower abdomen and right groin, Unknown
Physical examination (20-Sep-2013): Renal capsule not painful to pulse regularly, Unknown
Rest ECG: Overtightened left type left anterior hemiblock, Unknown
Transthoracic echocardiography(18-Sep-2013): Without regional wall movement interferences, Unknown
Transthoracic echocardiography(18-Sep-2013):No pericardial effusion, relaxation interference, Unknown
Transthoracic echocardiography(18-Sep-2013):Mitral, tricuspid, pulmonary valve morphological, Unknown
Transthoracic echocardiography(18-Sep-2013):Left inconspicuous ventricular resting function, Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. The patient had no history of smoking. Medical history included hypertension since 1980, chronic gastrointestinal disease described as collagenic colitis since 1995, ischemic heart disease since 2000, atrial fibrillation from Jan-2006 until Jan-2009, diabetes mellitus since 2006, hyperlipoproteinemia and hyperlipidemia before 2008, and peripheral arterial disease since 2008. The patient was not, at any time, exposed to any other erythropoetin-stimulating agent (ESA). Race/Ethnicity: Caucasian 18-Oct-2013: English translation of the discharge letter from the physician was received. Additional information was received regarding the patient's medical history. The patient's diabetes mellitus was described as type 2 currently dietary adjusted and hypertension was described as essential arterial hypertension. The patient had a history of exnicotine abuse. Other medical history of the patient included; 3 vessel coronary artery disease described as coronary 1-vessel disease MLTR diagonalis 1 - closure/recanalization attempt in 2003; history of N.Z tachyarrythmia absoluta in Jan-2004; serious mixed sleep apnea syndrome first diagnosed in January 2011 (no therapy because of masked gastrointestinal intolerance); Z.n pneumonia left in Mar-2011; hyperuricemia with gout of both feet in Apr-2011; chronic nephropathy III also reported as chronic renal failure STSD III with comp. a hypertensive vascular injury with renal anemia; benign prostatic hyperplasia, atrophic gastritis, known multifactorial anemia with vitamin B12 deficiency and renal insufficiency; polysegmental bony narrowing of the spinal canal and the neural foramina from L3/4 caudally; and previous cover plate compression fracture L2 and break of the cover plate also at L1 with appropriate reparation spondylophytes; secondary hyperparathyroidism; metabolic acidosis; infrarenal abdominal aortic aneurysm, dia. 2.73 cm in Aug-2013; and Budenofalk therapy. 04-Jun-
Unknown to Ongoing	Relevant Med History	Benign prostatic hyperplasia (Benign prostatic hyperplasia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History collagenic colitis; 1995	Colitis collagenous (Colitis microscopic);
Unknown to Ongoing	Relevant Med History	Nephropathy (Nephropathy);
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Vascular injury (Vascular injury);
Unknown to Ongoing	Relevant Med History 2006; currently dietary adjusted	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History 1980	Essential hypertension (Essential hypertension);
Unknown to Ongoing	Relevant Med History before 2008	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History before 2008	Hyperlipoproteinemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History 2000	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Anemia B12 deficiency (Anaemia vitamin B12 deficiency);
Unknown to Ongoing	Relevant Med History 2008	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Renal insufficiency (Renal failure);
Unknown	Relevant Med History Jan-2006 to Jan-2009	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Atrophic gastritis (Chronic gastritis);
Unknown	Relevant Med History	Nicotine abuse (Tobacco abuse);
Unknown	Relevant Med History	Gout (Gout);
Unknown	Relevant Med History	Hyperuricemia (Hyperuricaemia);
Unknown	Relevant Med History Aug-2013	Abdominal aortic aneurysm (Aortic aneurysm);
Unknown	Relevant Med History	Metabolic acidosis (Metabolic acidosis);
Unknown	Relevant Med History Mar-2011	Pneumonia (Pneumonia);
Unknown	Relevant Med History	Spinal stenosis of lumbar region (Lumbar spinal stenosis);
Unknown	Relevant Med History	Compression fracture (Compression fracture);
Unknown	Relevant Med History	Orthopedic procedure (Orthopaedic procedure);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown	Relevant Med History Jan-2011	Apnea syndrome (Sleep apnoea syndrome);
Unknown	Relevant Med History Jan-2004	Tachyarrhythmia absoluta (Atrial fibrillation);
Unknown	Past Drug Event	BUDENOFALK (BUDENOFALK); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SPAIN	20	FEB	1946	67 Years	Female	Unk	06	JUN	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ACVA [Cerebrovascular accident]
Sepsis [Sepsis]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Spain, administered subcutaneously for the treatment of renal anaemia. This report describes a case of ACVA.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 27-JAN-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) Freq: 1 Month; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) ERC (Drug therapy)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 30-OCT-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACREL (RISEDRONATE SODIUM) ; Unknown
#2) ANAKINRA (ANAKINRA) ; Unknown
#3) CRESTOR (ROSUVASTATIN CALCIUM) ; Unknown
#4) DACORTIN (PREDNISONE) ; Unknown
#5) FEBUXOSTAT (FEBUXOSTAT) ; Unknown
#6) SINTROM (ACENOCOUMAROL) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2091030

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-MAR-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This
serious case from a physician (Es-046-0003) describes a 67-year-old female patient (height: 155 cm) who received Retacrit (epoetin zeta; subcutaneous, once a month; batch number unknown; dose not reported) on 30-Oct-2011 for ERC .
Medical history included recent pregnancy, an unspecified positive family history, hyperlipidemia, hypertension, atrial fibrillation, previous use of alcohol in 2007, gouty arthritis, immunosupression, and immobilization. It was reported that the patient stayed on a chair almost all day. The patient was not exposed to any other erythropoetin-stimulatin agent. Concomitant medications included steroids, anakinra, Acrel, Dacortin, febuxostat, Zaldiar, vitamin D 1/OH, Crestor, Sintrom, omeprazole, atenolol, enalapril, and Zemplar (doses and routes of administration not reported), all for unknown indications. On 30-Oct-2011, the patient started treatment with epoetin zeta. Hemoglobin on 07-Dec-2012 was 13.6 g/dL. On an unknown date, frequency of epoetin zeta was changed from once a week to once a month. It was reported that the patient did not come to remission on Mar-2013. Last dose of epoetin zeta prior to the event was administered on 11-May-2013. On 06-Jun-2013, the patient was hospitalized due to ACVA on posterior cerebral artery (left) with confusional syndrome. The adverse event was further described as subacute cerebral ischemic lesion extensive posterior left under cranial MRI. Treatment for the adverse event included an anticoagulant, Acenocoumarol (dose and route of administration not reported). It was reported that hemoglobin of the patient at the time of the event was at 10.6 g/dL. On an unknown date, blood pressure was 162/100 (unit of measurement and normal values not reported). Action taken with epoetin zeta was not reported. On 03-Jul-2013, the patient recovered from the adverse event and was discharged from the hospital.
Laboratory data on 28-Nov-2013 included haemoglobin of 11.9, haematocrit of 37.9, reticulocytes of 0.76%, red blood cells of 4.81 x 10^6, and leukocytes of 17.700 (units of measurement and normal values not reported. The reporter's causality assessment of the event of ACVA in relation to epoetin zeta was unlikely. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and expiry date. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered. 10-Mar-2014: Follow-up information was received from the same reporter. Follow-up report was created to reflect new information obtained. Fatal sepsis was added as adverse event. On an unknown date, the patient had sepsis. Treatment for the event and action taken with the suspect drug were not reported. On 27-Jan-2014, the patient died. Cause of death was sepsis. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal sepsis in relation to epoetin zeta was not reported.

Case Comment: Overall case causality: Possible Although patient has significant risk cardiovascular risk factors, the suspect drug can theoretically increase the risk of thrombosis by increasing red blood cell concentration, so cannot totally rule out its possible contributory effects. - N. Gonzales (23 Dec 2013) Follow-up (24 Mar 2014): No change in previous company assessment for ACVA. Sepsis is not assessable. Cannot provide event causation without objective clinical event details . - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood pressure measurement	162/100,Unknown	
2	28-NOV-2013	Haematocrit	37.9,Unknown	
3	07-DEC-2012	Haemoglobin	13.6 g/dl	
4	06-JUN-2013	Haemoglobin	10.6 g/dl	
5	28-NOV-2013	Haemoglobin	11.9,Unknown	
6		Magnetic resonance imaging brain	posterior left,Unknown	
7		Magnetic resonance imaging brain	subacute cerebral ischemic lesion,Unknown	
8	28-NOV-2013	Red blood cell count	4.81 x 10^6,Unknown	
9	28-NOV-2013	Reticulocyte count	0.76 %	
10	28-NOV-2013	White blood cell count	17.700,Unknown	

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ZALDIAR (PARACETAMOL, TRAMADOL HYDROCHLORIDE) ; Unknown

#8) ZEMPLAR (PARICALCITOL) ; Unknown

#9) ATENOLOL (ATENOLOL) ; Unknown

#10) CORTICOSTEROIDS ; Unknown

#11) ENALAPRIL (ENALAPRIL) ; Unknown

#12) OMEPRAZOLE (OMEPRAZOLE) ; Unknown

#13) VITAMIN D /00107901/ (ERGOCALCIFEROL) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and tobacco usage were not reported. Medical history included recent pregnancy, an unspecified positive family history, hyperlipidemia, hypertension, atrial fibrillation, previous use of alcohol in 2007, gouty arthritis, immunosupression, and immobilization. It was reported that the patient stayed on a chair almost all day. The patient was not exposed to any other erythropoetin-stimulatin agent. Race/ethnicity: Caucasian On 27-Jan-2014, the patient died. Cause of death was sepsis. It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Gouty arthritis (Gouty arthritis);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Immobile (Immobile);
Unknown to Ongoing	Relevant Med History	Immunosuppression (Immunosuppression);
Unknown	Relevant Med History	Alcohol use (Alcohol use);
Unknown	Relevant Med History	Pregnancy (Pregnancy);
Unknown	Relevant Med History	Familial risk factor (Familial risk factor);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	01	JUN	1934	79 Years	Female	59.00 kg	29	DEC	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Angina pectoris [Angina pectoris]
Endstage renal disease failure [End stage renal disease]
NSTEMI [Acute myocardial infarction]
Cardiac failure with asystolia [Cardiac arrest]
Cardiac failure with asystolia [Cardiac failure]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of endstage renal

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 21-APR-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, Freq: 3 Week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 16-JAN-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS 1 A PHARMA (ACETYLSALICYLIC ACID) Tablet ; Unknown
#2) BISOPROLOL AL (BISOPROLOL FUMARATE) Tablet ; Unknown
#3) CALCIUMACETAT NEFRO (CALCIUM ACETATE) Tablet ; Unknown
#4) CARENAL (BIOTIN, FOLIC ACID, NICOTINIC ACID, PANTOTHE
#5) DIGIMED (DIGITOXIN) Tablet ; Unknown
#6) EBRANTIL /00631801/ (URAPIDIL) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2117697

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

disease failure, angina pectoris, and thromboembolic events. This serious case from an investigator (reference: Ge-165-0007) describes a 79-year-old female patient (weight: 59 kg and height: 164 cm) who received Retacrit (epoetin zeta, subcutaneous, three times a week, batch number unknown; dose not reported) for renal anaemia from 16-Jan-2013. Medical history included hyperlipidemia, ischemic heart disease, transient ischemic attack, and hypertension. The patient's BMI was 23.05 kg/m^2. The patient previously received Aranesp 30 mcg and Neorecormon 2000 IE, routes of administration not reported; but did not experience any thromboembolic event during treatment. Concomitant medications included furosemid 125 1A Pharma tablet (1-1-0-0, dose not reported), bisoprolol Al coated tablet (5 mg, 1-0-1-0), calcium acetate Nefro coated ablet (500 mg, 1-1-1-1, with meals), ramipril 1A Pharma tablet (5 mg, 0-1-1-0), Nepresol tablet (25 mg , 1-1-1-0), Ebrantil 30 prolonged release capsule (as requred if RR is about 180 mmHg, dose not reported), Digimed 0.07 tablet (1-0-0-0, dose not reported), ASS 100 1A Pharma TAH tablet (1-0-0-0, dose not reported), Nexium enteric resistance tablet (40 mg , 1-0-0-0), Novaminsulfon Ratio. tablet (500 mg, 0-1-0-1), hydromorphon Al prolonged release tablet (4 mg , 1/2-0-1/2-0), Carenal coated tablet (1-0-0-0, dose not reported), Movicol Beutel Pulver (need; dose not reported), and simvastatin 1A Pharma coated tablet (60 mg, 0-0-1-0); routes of administration not reported, all for unknown indications. On 16-Jan-2013, the patient started treatment with epoetin zeta. The patient received the last dose prior to the adverse event on 28-Dec-2013. On an unknown date, the patient experienced thromboembolic events. On 29-Dec-2013, the patient experienced end stage renal disease and angina pectoris and was hospitalised. The patient laboratory tests on 30-Dec-2013 at 13:08 included haematocrit of 28 % (normal: 34.1-44.9); potassium of 4.5 mmol/l, sodium serum 135 mmol/l, and calcium serum 1.15 mmol/l, normal values not reported. Action taken with suspect drug was not reported. Treatment for the events included coronary angiography and drug eluting stent. Outcome of the events of endstage renal disease failure and angina pectoris was ongoing at the time report while not reported for thromboembolic events. The reporter's causality assessment for the events of end stage renal disease failure and angina pectoris in relation to epoetin zeta was not related while not reported for thromboembolic events. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered.
14-Jan-2014: English translation of the German discharge letter was received. Follow up report was created to reflect additional information regarding suspect drug, laboratory and diagnostic tests and adverse events. The adverse event thromboembolic events was updated to NSTEMI. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: dosage administered. The patient received Retacrit at a dose of 4000 IE. On an unknown date, the patient was diagnosed with NSTEMI in conjuction with progression of coronary heart disease. On an unknown date, haemodynamics showed HR of 76 1/min (normal values not reported) and AO of 168/59/105 (units and normal values not reported). Coronary angiography revealed the following:
main stem: high grade in-stent stenosis; LAD: high-grade ostial stenosis and high grade extensive stenosis of the entire LAD. Only negligible competitive flow at the insertion site of the LIMA bypass; RCX: high-grade stenosis near the origin of the R.m.I; RCA: ostial in-stent thrombosis with high-grade stenosis; LIMA – LAD: high-grade in-stent stenosis just before the insertion into LAD. Very reluctant flow at CM, functionally occluded vessel; ACVB – R.m.II: successful venous bypass. Intervention given included successful DES-PTCA of the ostium RCA and two successful DES-PTCA of the main coronary artery and the LAD. Additional procedures included ASA 100mg/d for life, Ticagrelor 2x90 mg/day for 12 months, monitoring of risk factors, dialysis as scheduled, in the event of larger haematoma, pressure band for 8 h to 19:00 following administration of Integrilin. On 29-Dec-2013 at 16:39 laboratory tests revealed CK 54 U/l (normal range: 1-200), CK-MB 14 U/l (normal: 1-24), CK-MB prop. 1 % (normal: 1-6), and troponin T hs was 973++ and 173++ pg/ml (normal: less than 14). On 30-Dec-2013 at 07:49 investigations revealed creatinine 3.03+ mg/dl (normal: 0.5-0.9), e-GFR 16- ml/min (normal: 80-140), sodium 142 mmol/l (normal: 132-155), potassium 5.03 mmol/l (normal: 3.3-5.5), CK 51 U/l, CK-MB 11 U/l, CK-MB prop. 1 %, erythrocytes 3.66- 10^6/mcL (normal: 4.0-5.3), haemoglobin 11.0- g/dl (normal: 12.0-16.0), haematocrit 35.0- % (normal: 37-47), thrombocytes 307 10^3/mcL (normal: 140-400), PTT 24- sec (normal: 26-33), Quick greater than 100 % (normal: 82-130), INR 1.00 (normal: 0.86-1.27), and troponin T hs 923++ and 123++ pg/ml. On 31-Dec-2013 at 08:20 investigations revealed creatinine 3.07+ mg/dl, e-GFR 16- ml/min, sodium 141 mmol/l, potassium 5.02 mmol/l, CK 246+ U/l, CK-MB 40- U/l, CK-MB prop. 16.3+ %, erythrocytes 3.14- 10^6/mcL, haemoglobin 9.3- g/dl, haematocrit 30.4- %, thrombocytes 346 10^3/mcL, PTT 23- sec, Quick 87 %, INR 1.09, and troponin T hs 1304++ pg/ml. On the same day at 17:43, additional laboratory tests included CK 229+ U/l, CK-MB 31+ U/l, CK-MB prop. 13.5+ %, and troponin T hs 947++ pg/ml. On 01-Jan-2014 at 15:02, laboratory tests included creatinine 4.29+ mg/dl, e-GFR 11- ml/min, sodium 140 mmol/l, potassium 4.47 mmol/l, calcium 2.17 mmol/l, CK 153 U/l, CK-MB 24 U/l, CK-MB prop. 1%, erythrocytes 2.93-- 10^6/mcL, haemoglobin 8.9- g/dl, haematocrit 28.2 %, thrombocytes 374 10^3/mcL, PTT 22 sec, Quick 93 %, and INR 1.05. On the same day at 22:50, the patient's PTT was 55++ sec, Quick 74- %, and INR of 1.19+.
On 02-Jan-2014, investigations showed PTT was greater than 120++k sec, Quick 39-- %, and INR 1.88+ at 18:36; and PTT greater than 120++ sec, Quick 61- %, and INR 1.34+ at 19:52. Transthoracic echocardiography (TTE) on 02-Jan-2014 revealed all HH with normal breadth, LV wall thickness hypertophied, overall borderline normal systolic LV function with no regional abnormalities detected in the movement of the heart wall, diastolic malfunctioning, normal morphology of the aortic valves, normal separation, no pathological gradients, small AI in the FD, mitral valve normal, normal separations, no Mi, no PE, small TI, and mild pHT (35 mmHg plus CVD). In summary: normal systolic LV function with no regional abnormalities in the movement of the heart wall, LV hypertrophy, relaxation disturbance and mild pHT. On 03-Jan-2014 at 08:12, laboratory tests included creatinine 3.69+ mg/dl, e-GFR 13- ml/min, sodium 143 mmol/l, potassium 4.45 mmol/l, CK 68 U/l, CK-MB 14 U/l, CK-MB prop. 1%, erythrocytes 3.11- 10^6/mcL, haemoglobin 9.3- g/dl, haematocrit 29.7- %, thrombocytes 403+ 10^3/mcL, PTT 51++ sec, Quick 88 %, and INR 1.08. 21-Apr-2014: Follow up information was received from the same reporter. Follow up report was created to reflect additional information regarding adverse events. Fatal cardiac failure with asystolia was added as adverse event. On an unknown date, the

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

patient experienced cardiac failure with asystolia. Treatment for the adverse events was not reported. On 21-Apr-2014, the patient died. Cause of death was cardiac failure with asystolia. It was not reported if an autopsy was performed.
The reporter's causality assessment for the event of cardiac failure with asystolia in relation to Retacrit was not related. It was reported that cardiac failure were coronary heart disease and kidney failure.

Case Comment: Overall case causality: Possible The end stage renal disease and angina are preexistent conditions and not related to the study drug. The thrombopembolic events are possibly related. Suspect drug can theoretically increase the risk of thrombosis by increasing red blood cell concentration. Consider also contributory effects of preexistent cardiovascular conditions and risk factors. - N. Gonzales (09 Jan 2014) Follow-up: No change in previous causality assessment. - N. Gonzales (21 Jan 2014) Follow-up (25 Apr 2014): No change in assessment for previous events. Cardiac failure with asystolia is probably not related. Noting reporter's assessment, the event is more likely due to the patient's underlying cardiac and renal problems. - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-DEC-2013	Activated partial thromboplastin time	24- seconds	33 26
2	31-DEC-2013	Activated partial thromboplastin time	23- seconds	33 26
3	01-JAN-2014	Activated partial thromboplastin time	55++ seconds	33 26
4	01-JAN-2014	Activated partial thromboplastin time	22 seconds	33 26
5	02-JAN-2014	Activated partial thromboplastin time	greater than 120++ seconds	33 26
6	02-JAN-2014	Activated partial thromboplastin time	greater than 120++k seconds	33 26
7	03-JAN-2014	Activated partial thromboplastin time	51++ seconds	33 26
8		Angiocardiogram	RCA: ostial in-stent thrombosis, Unknown	
9		Angiocardiogram	RCA: with high-grade stenosis, Unknown	
10		Angiocardiogram	RCX: high-grade stenosis near origin of R.m.I, Unk	
11		Angiocardiogram	Main stem: high grade in-stent stenosis, Unknown	
12		Angiocardiogram	LIMA-LAD: Very reluctant flow at CM, Unknown	
13		Angiocardiogram	LAD: negligible competitive flow, Unknown	
14		Angiocardiogram	LAD: high-grade ostial stenosis, Unknown	
15		Angiocardiogram	LAD: High grade extensive stenosis of entire LAD,	
16		Angiocardiogram	LAD: at the insertion site of the LIMA bypass Unkn	
17		Angiocardiogram	LIMA-LAD: functionally	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			occluded vessel, Unknown	
18		Angiocardiogram	LIMA-LAD: high-grade in-stent stenosis, Unknown	
19	30-DEC-2013	Blood calcium	1.15 mmol/l	
20	01-JAN-2014	Blood calcium	2.17 mmol/l	2.8 2.0
21	29-DEC-2013	Blood creatine phosphokinase	54 IU/l	200 1
22	30-DEC-2013	Blood creatine phosphokinase	51 IU/l	200 1
23	31-DEC-2013	Blood creatine phosphokinase	246+ IU/l	200 1
24	31-DEC-2013	Blood creatine phosphokinase	229+ IU/l	200 1
25	01-JAN-2014	Blood creatine phosphokinase	153 IU/l	200 1
26	03-JAN-2014	Blood creatine phosphokinase	68 IU/l	200 1
27	29-DEC-2013	Blood creatine phosphokinase MB	14 IU/l	24 1
28	29-DEC-2013	Blood creatine phosphokinase MB	1 %	6 1
29	30-DEC-2013	Blood creatine phosphokinase MB	1 %	6 1
30	30-DEC-2013	Blood creatine phosphokinase MB	11 IU/l	24 1
31	31-DEC-2013	Blood creatine phosphokinase MB	16.3+ %	6 1
32	31-DEC-2013	Blood creatine phosphokinase MB	31+ IU/l	24 1
33	31-DEC-2013	Blood creatine phosphokinase MB	40- IU/l	24 1
34	31-DEC-2013	Blood creatine phosphokinase MB	13.5+ %	6 1
35	01-JAN-2014	Blood creatine phosphokinase MB	24 IU/l	24 1
36	01-JAN-2014	Blood creatine phosphokinase MB	1 %	6 1
37	03-JAN-2014	Blood creatine phosphokinase MB	14 IU/l	24 1
38	03-JAN-2014	Blood creatine phosphokinase MB	1 %	6 1
39	30-DEC-2013	Blood creatinine	3.03+ mg/dl	0.9 0.5
40	31-DEC-2013	Blood creatinine	3.07+ mg/dl	0.9 0.5
41	01-JAN-2014	Blood creatinine	4.29+ mg/dl	0.9 0.5
42	03-JAN-2014	Blood creatinine	3.69+ mg/dl	0.9 0.5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
43	30-DEC-2013	Blood potassium	4.5 mmol/l	
44	30-DEC-2013	Blood potassium	5.03 mmol/l	5.5 3.3
45	31-DEC-2013	Blood potassium	5.02 mmol/l	5.5 3.3
46	01-JAN-2014	Blood potassium	4.47 mmol/l	5.5 3.3
47	03-JAN-2014	Blood potassium	4.45 mmol/l	5.5 3.3
48	30-DEC-2013	Blood sodium	135 mmol/l	
49	30-DEC-2013	Blood sodium	142 mmol/l	155 132
50	31-DEC-2013	Blood sodium	141 mmol/l	155 132
51	01-JAN-2014	Blood sodium	140 mmol/l	155 132
52	03-JAN-2014	Blood sodium	143 mmol/l	155 132
53	02-JAN-2014	Echocardiogram	With no regional abnormalities, Unknown	
54	02-JAN-2014	Echocardiogram	In the movement of the heart wall, Unknown	
55	02-JAN-2014	Echocardiogram	Relaxation disturbance, Unknown	
56	02-JAN-2014	Echocardiogram	Mild pHT, Unknown	
57	02-JAN-2014	Echocardiogram	Normal systolic LV function, Unknown	
58	02-JAN-2014	Echocardiogram	LV hypertrophy, Unknown	
59	30-DEC-2013	Glomerular filtration rate	16- ml/min	140 80
60	31-DEC-2013	Glomerular filtration rate	16- ml/min	140 80
61	01-JAN-2014	Glomerular filtration rate	11- ml/min	140 80
62	03-JAN-2014	Glomerular filtration rate	13- ml/min	140 80
63	30-DEC-2013	Haematocrit	35.0- %	47 37
64	30-DEC-2013	Haematocrit	28 %	44.9 34.1
65	31-DEC-2013	Haematocrit	30.4- %	47 37
66	01-JAN-2014	Haematocrit	28.2 %	47 37
67	03-JAN-2014	Haematocrit	29.7- %	47 37
68		Haemodynamic test	168/59/105, Unknown	

Mfr. Control Number: 2117697

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
69	30-DEC-2013	Haemoglobin	11.0- g/dl	16.0 12.0
70	31-DEC-2013	Haemoglobin	9.3- g/dl	16.0 12.0
71	01-JAN-2014	Haemoglobin	8.9- g/dl	16.0 12.0
72	03-JAN-2014	Haemoglobin	9.3- g/dl	16.0 12.0
73		Heart rate	76 1/min, Unknown	
74	30-DEC-2013	International normalised ratio	1.00, Unknown	1.27 0.86
75	31-DEC-2013	International normalised ratio	1.09, Unknown	1.27 0.86
76	01-JAN-2014	International normalised ratio	1.05, Unknown	1.27 0.86
77	01-JAN-2014	International normalised ratio	1.19+, Unknown	1.27 0.86
78	02-JAN-2014	International normalised ratio	1.88+ Unknown	1.27 0.86
79	02-JAN-2014	International normalised ratio	1.34+ Unknown	1.27 0.86
80	03-JAN-2014	International normalised ratio	1.08, Unknown	1.27 0.86
81	30-DEC-2013	Platelet count	307 X10**3/MCL	400 140
82	31-DEC-2013	Platelet count	346 X10**3/MCL	400 140
83	01-JAN-2014	Platelet count	374 X10**3/MCL	400 140
84	03-JAN-2014	Platelet count	403+ X10**3/MCL	400 140
85	30-DEC-2013	Prothrombin time	greater than 100 %	130 82
86	31-DEC-2013	Prothrombin time	87 %	130 82
87	01-JAN-2014	Prothrombin time	93 %	130 82
88	01-JAN-2014	Prothrombin time	74- %	130 82
89	02-JAN-2014	Prothrombin time	39-- %	130 82
90	02-JAN-2014	Prothrombin time	61- %	130 82
91	03-JAN-2014	Prothrombin time	88 %	130 82
92	30-DEC-2013	Red blood cell count	3.66- X10**6/MCL	5.3 4.0
93	31-DEC-2013	Red blood cell count	3.14- X10**6/MCL	5.3 4.0
94	01-JAN-2014	Red blood cell count	2.93-- X10**6/MCL	5.3 4.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
95	03-JAN-2014	Red blood cell count	3.11- X10**6/MCL	5.3 4.0
96	29-DEC-2013	Troponin T	973++ PG/ML	
97	29-DEC-2013	Troponin T	173++ PG/ML	
98	30-DEC-2013	Troponin T	123++ PG/ML	
99	30-DEC-2013	Troponin T	923++ PG/ML	
100	31-DEC-2013	Troponin T	1304++ PG/ML	
101	31-DEC-2013	Troponin T	947++ PG/ML	

13. Relevant Tests

Coronary angiography(Unknown date): LAD: at the insertion site of the LIMA bypass, Unknown
Coronary angiography(Unknown date): LAD: High grade extensive stenosis of entire LAD, Unknown
Coronary angiography(Unknown date): RCX: high-grade stenosis near origin of R.m.I, Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) CARENAL (BIOTIN, FOLIC ACID, NICOTINIC ACID, PANTOTHENIC ACID, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, SELENIUM, THIAMINE HYDROCHLORIDE, TOCOPHEROL, VITAMIN B12 NOS) Tablet ; Unknown

#7) FUROSEMID 1A PHARM (FUROSEMIDE) Tablet ; Unknown

#8) MOVICOL /01749801/ (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE) ; Unknown

#9) NEPRESOL /00007602/ (HYDRALAZINE HYDROCHLORIDE) Tablet ; Unknown

#10) NEXIUM /01479302/ (ESOMEPRAZOLE MAGNESIUM) Tablet ; Unknown

#11) NOVAMINSULFON-RATIOPHARM (METAMIZOLE SODIUM) Tablet ; Unknown

#12) RAMIPRIL 1A PHARMA (RAMIPRIL) Tablet ; Unknown

#13) SIMVASTATIN-1A PHARMA (SIMVASTATIN) Tablet ; Unknown

#14) HYDROMORPHONE HCL (HYDROMORPHONE HYDROCHLORIDE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included hyperlipidemia, ischemic heart disease, transient ischemic attack, and hypertension. The patient's BMI was 23.05 kg/m^2. The patient previously received Aranesp 30 mcg and Neorecormon 2000 IE, routes of administration not reported; but did not experience any thromboembolic event during treatment. Race/ethnicity: Caucasian 21-Apr-2014: Additional information was received from the same reporter. On 21-Apr-2014, the patient died. Cause of death was cardiac failure with asystolia. It was not reported if an autopsy was performed.

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Kidney failure (Renal failure);
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
16-APR-2012 to 05-SEP-2012	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
07-DEC-2012 to 11-JAN-2013	Past Drug Event	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GERMANY	27	MAR	1932	81 Years	Female	84.00 kg	07	AUG	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Anemia [Anaemia]
NSEMi [Acute myocardial infarction]
Cerebral ischemia [Cerebral ischaemia]
Thromboembolic Events [Embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 167 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 02-MAY-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) BISOPROLOL 1A PHARMA (BISOPROLOL FUMARATE) Coated tablet ; Unknown
#2) FENTANYL (FENTANYL) ; 03-MAY-2009 / Unknown
#3) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX)
#4) CALCIUM-D3 (CALCIUM CARBONATE, COLECALCIFEROL) Tablet
#5) MIRTAZAPIN (MIRTAZAPINE) Tablet ; 03-MAY-2009 / Unknown
#6) NOVALGIN /00169801/ (CAFFEINE, PARACETAMOL, PROPYPHENAZ **(Continued on Additional Information Page)**

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
DEC-2008 to Ongoing	Relevant Med History	Anemia (Anaemia) also reported as hyperchromic macrocytic anaemia of undetermined origin
Unknown to Ongoing	Relevant Med History	Arterial occlusive disease (Arterial occlusive disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2126673

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-JUL-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

This is a Non-Interventional Study report for protocol EPOE-09-11. This Hospira sponsored study report received from an investigator (ref: Ge-432-0004) which refers to a subject. The subject was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation of Retacrit (EPOETIN ZETA), administered subcutaneously for the treatment of renal anaemia. Relevant medical history was reflected in the subject history data field. Con-meds included AbZ 500 mg tablets, Resolor 1 mg coated tablets, bisoprolol 1A Pharma 1.25 mg coated tablets, ASA 1A Pharma 100 mg tablet, clopidogrel hydrochloride 1A Pharma 75 mg, pantoprazole, mirtazapin, Novalgin, fentanyl, Targin, lactulose, Macrogol, AbZ powder for preparation of injection solution, Ferrlecit, torasemid, alendronate sodium (ALENDRONATE), metamizole sodium (METAMIZOLE). On 02May2012, prior to the study, the subject started treatment with Retacrit (epoetin zeta, subcutaneous) for an unknown indication. On 19Nov2012, the subject enrolled to the study and the informed consent was signed. During week of enrollment, the subject received Retacrit (167 IU/kg/week, subcutaneous, 3 dosages per week) for renal anaemia.
Current dose of Retacrit reported as 4000 E, thrice weekly. The subject received the last dose of Retacrit on 16Jul2013 prior to the adverse event (AE). It was reported that the subject hospitalized from 17Jul2013 until 04Aug2013. On 31Jul2013, the subject experienced trauma described as sintering fracture spine. On the same day, abdominal CTR was done (see labs section) bone marrow puncture showed no evidence of MDS. On 02Aug2013, bone marrow puncture revealed no evidence for the time being of MDS, B12 and folic acid deficiencies were also ruled out. On 06Aug2013, macroscopic examination, iron staining, immunohistochemistry (CD20) bone marrow smear Peripheral blood and differential cytology analysis were, performed (see labs section). Differential blood count normal as far as possible. There was megaloblastic anaemia; hence folic acid and vitamin B12 levels should be carried out to definitively rule out an initial form of myelodysplastic syndrome. The criteria for MDS at this time were not met. On 07Aug2013, the subject experienced anemia described as progressive anemia. No treatment was given for the event of anemia. On the same day, lab tests included Hkt 27.9 % and 28.40 %, ERY 2.37 Mill/mcl, HB 9.10 g/dl, and LEUK of 9.10 Tsd/mcl. On 20Aug2013, the subject presented for internal admission with deteriorated general health, loss of appetite, worsened mobility. She had been discharged from the previous hospital, where she had been examined regarding anaemia on 04Aug2013. According to her son, findings from gastroscopy, colonoscopy, thoracic and abdominal CTs were all normal. A biopsy of the iliac crest indicated megaloblastic anaemia. On an unknown date, the subject fell while in the medical clinic and a pelvic X-ray was done. Subject came for mobilization and clarification of cognitive abilities. No legal supervision, no legal authority in place. Upon admission, the subject was in several reduced general health, adipose nutritional status, dehydrated, oedema in both legs. She had impaired/delayed cognitive ability and required help in sitting up, lying down and transfer. Initial walking attempt with Rollator therapy involved pain in the LWS radiating to left leg. Coronary showed rhythmic and heart tones pure. Pulmonary showed eupnoea with vesicular heart sounds. Abdomen with no tenderness on palpitation, no muscular guarding, regular peristaltic sounds, no resistance palpable. Peripheral pulse status included foot pulse cannot be felt on either side due to leg oedema. Normal neural status. Rectal findings normal with negative haemoccult test. ECG was performed (see labs section). On 26Aug2013 cranial CR was performed (see labs section). After normochromic macrocytic anaemia was established and deterioration of mobility after the last hospital stay and with issues of falling, the subject was admitted in the Geriatric Department for mobilisation and ADL training. Initially, the mobilisation proceeded with great difficulty due to functional and cognitive impairments and little self- motivation in therapy, so that the subject relied on a great deal of help. A restricted Mini-mental Test at 20 points and a Clock Test at only 5 points were indications of moderate cognitive impairment, the CT scan revealed no other evidence of secondary cause of dementia. Since there was no severe impairment in everyday activities, neurological connection and follow-up in 3-6 months were recommended in order to determine if dementia treatment was an option. Hb value of 3.5 mg/dl was calculated, which tended to fall over the course of the period. Haemorrhage sources were isolated. Renal function remained stable and at discharge on 04Sep2013, creatinine and GFR were obtained (see labs section) and body weight was 84 kg with the ongoing Torem (low dose). In ergo- and physiotherapeutic plan, the subject will be able to acquire low level of mobility. Nevertheless, the subject still required assistance in personal care/hygiene and ADL. On discharge, resilience, cognition, and self-motivation were reduced, but easily noticeable in treatment, change in position and transfers adequately possible with assistance, insecure when standing freely but sufficiently secure when held, walks with difficulty and uncoordinated for approximately 20 m with Rollator and supervision, unable to adequately walk secure on her own, handling of Rollator was unsure, subject did not want to attempt stairs. On 04Oct2013, the subject's lab tests included Hkt 26.9 % and 26.10 %, ERY 2.25 Mill/mcl and HB 8.50 g/dl. On 01Nov2013, lab tests included Hkt 26.8 % and 26.20 %, ERY 2.30 Mill/mcl and HB 8.50 g/dl. On 14Nov2013, the subject received the last dose of Retacrit prior to the event of (non-ST-elevation myocardial infraction) NSEMi. On 17Nov2013, the subject experienced NSEMi described as NSTEMI with following lung edema due to cardiac decompensation also reported as acute cardiogenic pulmonary oedema and was hospitalized on the same day. Physical examination included severely deteriorated general health, adipose nutritional status. Coronary, pulmonary and abdomen examinations were performed (see labs section). The subject had leg oedema on both sides. Basic neurological examination was with normal findings. ECG on admission and over the course of therapy showed alteration between internal rhythm (SR) and VVI stimulation, heart axis could not be determined during internal rhythm, complete RBBB, LAH; repolarisation disturbances caused by block. Echocardiography was also performed (see labs section). Coronary angiogram from 17Nov2013 revealed significant 90 % stenosis of the main stem branch extending to ostial Cx and LAD; 60 % stenosis of the RD1, 60 % stenosis of the distal LAD, significant 80% stenosis of the proximal RIM; significant stenosis of the RM1, and 60% stenosis of the med. RCA. Coronary angiogram from 18Nov2013 revealed the following: LMCA not shown again; significant, extensive 70 % stenosis of the med. RCA, significant 70 % stenosis of the ostial RCA and on 20Nov2013 showed the following: RCA still with good results after PCI a few days prior. As above coronary angiogram indicated severe 3-vessel coronary artery disease with significant stenosis of the main stem, such that cardiac recompensation took place first in the haemodynamically stable pt. This was immediately possible on the day of admission. Subsequently the pros and

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

cons of bypass surgery and interventional treatment of the disease were reviewed with the subject. The subject opted for an interventional approach. In two further appointments on 18Nov2013 and 20Nov2013, the significant stenosis had been taken care of interventionally. On 17Nov2013 at 17:32, the subject's lab tests included erythrocytes 2.74, haemoglobin (Hgb) 10.2, hematocrit (HCT) 31.5, thrombocytes (PLT) 264, Quick 105, INR 1.00, PTT 35, CK 109, CKMB 98, and troponin T 48.2 (units and normal values not reported). On the same day at 21:31 the subject's CK was 101 and CKMB 82. On 18Nov2013 at 07:27, lab tests included erythrocytes 2.35 Hgb 8.7, HCT 27.3, platelets (PLT) 235, Quick 90, INR 1.08, PTT 41, CK 89, CKMB 70, and troponin T 59.8.On 18Nov2013 at 15:08, lab tests included erythrocytes 2.48 Hgb 9.4, HCT 29.0, PLT 212, CK 97, and CKMB 54. On 19Nov2013 at 07:27, lab tests included erythrocytes 2.19 Hgb 8.1, HCT 25.8, PLT 209, Quick 88, INR 1.10, PTT 42, CK 127, and CKMB 59. On 20Nov2013 at 10:06, lab tests included erythrocytes 2.36, Hgb 3.1, HCT 28.3, PLT 216, Quick 100, INR 1.01, PTT 25, CK 115, and CKMB 71. On 22Nov2013 at 07:18, lab tests Hgb 7.4, HCT 23.9, PLT 209, Quick 94, INR 1.05, and PTT 43. On the same day of 22Nov2013 at 16:16, lab tests included erythrocytes 2.22, Hgb 8.2, HCT 26.0 and PLT 218. On 23Nov2013 at 10:17, lab tests included erythrocytes 2.29, Hgb 8.5, HCT 27.0 and PLT 220. On 25Nov2013 at 10:21, lab tests included erythrocytes 2.25, Hgb 8.2, HCT 25.9 and PLT 248. On 27Nov2013 at 10:41, lab tests included erythrocytes 2.38, Hgb 8.7, HCT 27.3, and PLT 269. Dual platelet aggregation inhibition using ASA and Clopidogrel was recommended for 12 months, if necessary deciding in 6 months about ASA and Marcumar. Another macrocytic hyperchromic anaemia was apparent in laboratory analyses, although Hb value continued to be stable. The folic acid deficiency was substituted. Vitamin B12 was not administered due to presently satisfactory levels, but should be rechecked 1x/month if necessary because of known B12 deficiency. The inpt progress after this proceeded without complication and even renal retention parameters regressed slightly (creatinine at 2.04 mg/dl). Body weight at discharge was 76.5 kg. Treatment for NSEMi included PTCA-RCA, and LCX, LAD, on 20Nov2013. At the time of the report, the outcome of the event of anemia was not recovered; while persistent/significant disability for the event of NSEMi with event end date reported as 27Nov2013. On the same day, the subject was discharged from the hospital. On 28May2015, Hb was at 9.0 g/dL. On 02Jun2015, Hb was at 8.8 g/dL. On 08Jun2015, the subject received the last dose of Retacrit prior to event. On 10Jun2015, the subject presented to the emergency admissions due to somnolence. The subject had been found sitting somnolent on the chair with hemiparesis of the right side, accentuated in the arm. During emergency admission, the subject was responsive and oriented in place but not in time. There was existing slight weakness of the right arm; the subject was in stable overall cardiopulmonary condition. Based on medical history compiled elsewhere, until this episode the subject was fully mobile, able to take care of herself and mobile with a wheelchair as well. Dementia was known in the prior medical history so the extent of orientation was not clear. According to the nursing home, the subject was still oriented in person, place and time. Physical examination was performed on admission showed she was in reduced overall condition and poor nutritional state. Heart, lungs breath sounds, abdomen and eyes were examined (see labs section). Temperature, BP, pulse, respiratory rate and oxygen saturation were taken (see labs section). In the next stages, a cranial CT was performed, compared to previous examination on 09Apr2015, status was unchanged, advanced microangiopathic changes were noted and slight generalised atrophy with no evidence of intracranial bleeding. No distinctive new signs of ischaemia as far can be seen in the image. On the same day, neurological consultation was sought (see labs section). Treatment for the cerebral ischemia included systemic lysis with Actilyse (63 mg, intravenous) that was carried out in a period of 2.5 h and restitution. It was reported that the symptoms and hemiparesis on the right improved somewhat with this treatment. It was also reported that the subject's chronic anaemia had remained stable under care after lysis therapy. The subject arrived with Hb value of 7.9 g/dL and 1 erythrocyte concentrate (RCC) was transfused. On 10Jun2015, investigations showed erythrocytes at 2.09 10S3/mcL (4.1-5.1), Hgb at 7.9 g/ dL (10.9-16.9), HCT at 2.7 fL (35.0-47.0), thrombocytes at 266 10S3/mcL (139-409), blood sedimentation at 64 mm/h (2-10), Quick ACLPRO at 107% (70-130), INR at 0.97 (1.0-1.24; unit of measurement not reported), aPTT ACL PRO at 21 sec (22-33), CRP at 13.65 mg/L (0.0-6.0), CPK at 56 U/L (0-145) and LDH at 126 U/L (110-247). On 11Jun2015, a follow up cranial CT was performed and showed that there was distinct demarcation of an extensive zone of ischaemia in the basal region of the left temporal lobe reaching as far as the basal ganglia; still no evidence of intracerebral bleeding; no significant pressure components and the area of the ischaemia is attributed to the posterior cerebral artery. INN duplex sonography of the carotids was also performed and showed both sides were calcified, plaque in the lumen bulbs/ (illegible) junction. There was narrowing of the lumen on the left with no evidence of a relevant stenosis; flow was 160-180 cm; weaker findings on the right, no flow acceleration, vertebralis on both sides normal; echocardiography was vehemently refused by the subject. Neurological consultation showed clinical posterior infarction with right sided homonymous hemiparesis; cardiovascular diagnostics was recommended and known paroxysmal atrial fibrillation was noted with CHADVASc score of 6 points and HAS-BLED score of 4 points meaning a relative contraindication for anticoagulants. These may be introduced three to four weeks depending on subject's progress. The subject was put in the intensive care ward from 10 to 11Jun2015. On 11Jun2015, she was transferred to standard care for further diagnosis and treatment. The subject was mobilised with physiotherapy and was successful making the subject able to move her right side somewhat more. On an unknown date, further, the lab chemistry works were performed and indicated increased inflammatory parameters. Also on an unknown date, transcranial Doppler was performed. On 12Jun2015 erythrocytes at 2.3 and 2.20 10S3/mcL, Hgb at 8.5 and 8.2 g/dL, HCT at 21.6 and 26.0 fL, thrombocytes (illegible) and 205 10s3/ mcL, CRP at 71.69 mg/L, CPK at 63 U/L and LDH at 135 U/L. On the same day, INN echocardiography was performed and showed that the left side heart cavities were not enlarged, no hypertrophy; normal LV function; right side heart cavities somewhat enlarged no localised (illegible) valves with FDE: slight aortic valve reflux with strong sclerosis (illegible) with PAH (illegible). On 13Jun2015, urinalysis was performed (see labs section) indicative of an incipient urinary tract infection which was treated with ciprofloxacin (250 mg, 1-0-1). It was also reported that the inflammatory parameters have regressed with time. On an illegible date, erythrocytes at 2.30 10S3/mcL, Hgb at 7.8 g/dL, HCT at 24.6 fL, thrombocytes at 185 10S3/ mcL, C-reactive protein (CRP) at 57.48 mg/L, CPK at 63 U/L and LDH at 121 U/L. Action taken with epoetin zeta was not applicable. On 16Aug2015, erythrocytes at 2.45 10S3/mcL, Hgb at 8.8 g/dL, HCT at 26.5 fL and thrombocytes at 187 10S3/ mcL. Outcome of the AE was recovered on 18Jun2015. On 18Aug2015, at 14:47 erythrocyte at 1.95 Mio/uL (3.9-5.2), hemoglobin was at 7.5 g/dL and hematokrit was at 23% (38-46). The reporter's opinion of causality for the event of anemia and cerebral ischemia the suspect drug was unlikely while not related for the event of NSEMi. Risk factors included obesity with BMI of 29.4, trauma described as sintering fracture spine also described as multifactorial chronic pain syndrome, immobilization, vascular anomalies described as peripheral arterial disease also reported as PAOD affecting pelvic arteries on the right, polymyalgia, atrial fibrillation, cerebrovascular disease, hyperlipidaemia, hypertension, and Type 2 diabetes mellitus without vascular complications controlled with diet HbA 1c 4.4%. 27Jan2014: English translation of the

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

German discharge letter was received. Follow up report was created to reflect additional information regarding medical history, concomitant medications, diagnostics, laboratory tests, and AEs. The active substance of Ideos was reported as calcium D-3. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and date of expiry. 26Aug2015: Additional information was received from the same reporter. Cerebral ischemia was added as an AE. Dose, frequency, and indication of Retacrit and date of last dose of Retacrit prior to cerebral ischemia were provided. Obesity with BMI of 29.4, trauma described as sintering fracture spine also described as multifactorial chronic pain syndrome, immobilization, vascular anomalies described as peripheral arterial disease also reported as PAOD affecting pelvic arteries on the right, polymyalgia, atrial fibrillation, cerebrovascular disease, hyperlipidaemia, hypertension, and Type 2 diabetes mellitus without vascular complications controlled with diet HbA 1c 4.4% were reported as risk factors. Targin was added as concomitant medication. Indication and frequency of torasemid; doses, frequencies and therapy dates of clopidogrel, Macrogol and ASA were updated and indication of clopidogrel hydrochloride and ASA were provided. Date of enrollment to study, further hospitalisation and AE details were also provided. Laboratory/diagnostic data on 28May2015, 02Jun2015, and 18Aug2015 were provided. MedDRA code of lab tests iron staining, peripheral blood, abdomen and LEUK were updated from blood test, physical examination and leukocyte count NOS to iron, blood smear test, gastrointestinal examination and leucocyte count respectively. This information has been incorporated in the narrative and in the corresponding data fields. 09Sep2015: English translation of German discharge letter was received. Chronic interstitial nephritis, hypertriglyceridaemia, liver parenchyma damage, hypertensive heart disease, cerebral sclerosis, pelvic ring fracture, psoriasis, exclusion of PRCA in Jan2014, status post-surgery for a retroperitoneal fistula abscess on the right with relationship to right kidney and right psoas major, MRSA wound infection, hiatus hernia, status post laparoscopic adhesiolysis, status post incisional hernia plastics and pangastritis were added as medical history. Laboratory and diagnostic tests on 10, 11, and 12Jun2015; 18Aug2015 were added. This information has been incorporated in the narrative and in the corresponding data fields. As of 01Jul2019, it was reported events anemia, thromboembolic events and acute myocardial infarction were not reported. Physician confirmed "thromboembolic events" was a reportable event. The corresponding event NSTEMI (onset date 17Nov2013) was already reported in year 2014. Normal ranges for "erythrocytes" and "C-reactive protein" were received from two different laboratories. Normal range "erythrocyte" 3.9 - 5.2 mio/ul (laboratory from general practitioner) and 4.1 - 5.1 mio/ul (laboratory of reporting physician). Normal range "CRP" 0.0 - 0.6 mg/l (laboratory value form hospital report) and 0.0 - 0.0 mg/l (laboratory of reporting physician, normal values is negative < 5). The dosage regimen of EPOETIN Zeta reported as first dose on 02May2012, last dose before event on 08Jun2015, frequency 3 x weekly via subcutaneous route of administration, information regarding dose: main dose 1 12000 units on 07Jun2015 (hemoglobin 8.8 g/dl) and main dose 2 12000 units on 18May2015 (hemoglobin 9.0 g/dl), dose was not changed within last 3 months prior to SAE. Other Erythropoetin stimulating agents included MIRCERA (27Oct2009 - 07Apr2010, dose 75 -120, hemoglobin 8.5 - 9.2 g/dl) and ARANESP (21Apr2010 - 15Mar2012, dose 50 - 150, hemoglobin 8.4 - 12.2 g/dl). No events occurred under other Erythropoetin stimulating agents. Risk factors for thromboembolic events included obesity (ongoing, BMI 29.4), trauma (31Jul2013 and ongoing, sintering fracture spine), vessel anomaly (unknown start date and ongoing, peripheral arterial disease), Immobilisation (from 04Aug2006 and ongoing). Other risk factors included diabetes (01Sep2005 and ongoing) and hypertension (01Sep2005 and ongoing) and polymyalgia (01Dec2008 and ongoing). Relevant medical history included hyperlipidemia (unknown start date, ongoing), ischemic heart disease (unknown start date, ongoing), peripheral arterial disease (May2006 and ongoing), diabetes mellitus (Sep2005 and ongoing), hypertension (Sep2005 and ongoing), atrial fibrillation (unknown start date and ongoing), chronic gastrointestinal disease (recurrent gastritis, unknown start date and ongoing), and osteoporosis (Aug2006 and ongoing).Laboratory tests (25Mar2015; only abnormal tests): HAPT (haptoglobin) 257.00 mg/dl (increased), Creatinine 2.60 mg/dl (increased), CRP 60.00 mg/l (increased), erythrocytes 1.94 mio/ul (decreased), GFR 19.00 (decreased), hemoglobin 6.80 g/dl (decreased), hematocrit 21.40 % (decreased), uric acid 8.37 mg/dl (increased), urea 102.00 mg/dl (increased), MCH 35.10 pg (increased), MCHC 31.80 g/dl (decreased), MCV 110.00 fl (increased), and reticulocytes 18.00 (increased). Laboratory tests (08Apr2015; only abnormal tests): alkaline phosphatase 189.00 U/l (increased), Creatinine 2.80 mg/dl (increased), CRP 18.00 mg/l (increased), Erythrocytes 1.89 mio/ul (decreased), ferritin 591.00 ug/l (increased), GFR 17.00 (decreased), GGT 64.00 U/l (increased), hemoglobin 6.70 g/dl (decreased), hematocrit 21.20 % (decreased), uric acid 9.43 mg/dl (increased), urea 97.00 mg/dl (increased), MCH 35.40 pg (increased), MCHC 31.60 g/dl (decreased), MCV 112.00 fl (increased), and reticulocytes 22.00 (increased). Laboratory tests (21Apr2015; only abnormal tests): creatinine 2.56 mg/dl (increased), CRP 20.00 mg/l (increased), erythrocytes 2.45 mio/ul (decreased), GFR 19.00 (decreased), hemoglobin 8.30 g/dl (decreased), hematocrit 26.50 % (decreased), uric acid 8.97 mg/dl (increased), urea 90.00 mg/dl (increased), MCH 33.90 pg (increased), MCHC 31.30 g/dl (decreased), MCV 108.00 fl (increased), and reticulocytes 17.00 (increased). Laboratory tests (07May2015; only abnormal tests): Creatinine 2.41 mg/dl (increased), CRP 7.00 mg/l (increased), erythrocytes 2.55 mio/ul (decreased), GFR 20.00 (decreased), hemoglobin 8.70 g/dl (decreased), hematocrit 27.70 % (decreased), uric acid 8.59 mg/dl (increased), urea 112.00 mg/dl (increased), potassium 3.40 mmol/l (decreased), MCH 34.10 pg (increased), MCHC 31.40 g/dl (decreased), MCV 109.00 fl (increased), and reticulocytes 18.00 (increased). Laboratory tests (18May2015; only abnormal tests): creatinine 2.44 mg/dl (increased), erythrocytes 2.55 mio/ul (decreased), GFR 20.00 (decreased), hemoglobin 9.00 g/dl (decreased), hematocrit 27.90 % (decreased), uric acid 8.29 mg/dl (increased), urea 124.00 mg/dl (increased), potassium 3.40 mmol/l (decreased), MCH 35.30 pg (increased), MCHC 32.20 g/dl (decreased), MCV 109.00 fl (increased), and reticulocytes 17.00 (increased). Laboratory tests (02Jun2015; only abnormal tests): cholesterol 253.00 mg/dl (increased), creatinine 3.16 mg/dl (increased), CRP 6.00 mg/l (increased), erythrocytes 2.44 mio/ul (decreased), GFR 15.00 (decreased), hemoglobin 8.80 g/dl (decreased), hematocrit 27.00 % (decreased), uric acid 9.16 mg/dl (increased), urea 141.00 mg/dl (increased), MCH 36.10 pg (increased), MCHC 32.60 g/dl (decreased), MCV 111.00 fl (increased), and triglycerides 351.00 mg/dl (increased).
Laboratory tests (18Aug2015; only abnormal tests): hemoglobin 7.5 g/dl (normal 12-16), hematocrit 23 % (normal 36-46), GFR 15 ml/min (normal >60).

The reporter's considered that there was not a reasonable possibility that the event cerebral ischemia was related to the study drug and the concomitant medication. The reporter's assessment of the causal relationship of the event thromboembolic events with the suspect products was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Follow-up (29Mar2019 and 30Mar2019): New information reported includes: AE of special interest data updated from "Lack of Efficacy: Thromboembolic Events" to "Thromboembolic Events", but it also reported the report belongs to the Event "Anemia" and reported no lack of efficacy occurred.

Follow-up (07Jun2019): New information reported includes: new event 'Thromboembolic Events' was reported, but the event onset/stop date, seriousness criteria, outcome, causality to study drug and concomitant drugs were not reported.

Follow-up (17Jun2019): New information reported included: study drug information (action taken updated).

Follow-up (01Jul2019): New information received from the physician in response to open queries included: suspect drug dosage regimen, event details (confirm "thromboembolic events" was a reportable event), relevant medical history and lab data.

Case Comment: The events Anemia, NSEMi, Cerebral ischemia and Thromboembolic events are most likely related to intercurrent or underlying conditions and unrelated to suspect drug EPOETIN ZETA. Patient's cardiovascular risk factors including Arterial occlusive disease and history of Macrocytic anaemia and history of trauma may have played a contributory role.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	17-NOV-2013	Activated partial thromboplastin time	35, Unknown	
2	18-NOV-2013	Activated partial thromboplastin time	41, Unknown	
3	19-NOV-2013	Activated partial thromboplastin time	42, Unknown	
4	20-NOV-2013	Activated partial thromboplastin time	25, Unknown	
5	22-NOV-2013	Activated partial thromboplastin time	43, Unknown	
6	17-NOV-2013	Angiocardiogram	Extending to ostail Cx and LAD, Unknown	
7	17-NOV-2013	Angiocardiogram	60% stenosis of the RD1, Unknown	
8	17-NOV-2013	Angiocardiogram	60% stenosis of the med. RCA, Unknown	
9	17-NOV-2013	Angiocardiogram	Significant 90% stenosis of the RM1, Unknown	
10	17-NOV-2013	Angiocardiogram	Significant 80 % stenosis of the proximal RMI, Un	
11	17-NOV-2013	Angiocardiogram	Significant 90% stenosis of the main stem branch,	
12	17-NOV-2013	Angiocardiogram	60% stenosis of the distal LAD, Unknown	
13	18-NOV-2013	Angiocardiogram	Significant 70% stenosis of the ostial RCA, unkno	
14	18-NOV-2013	Angiocardiogram	Significant extensive 70% stenosis of the med. RCA	
15	18-NOV-2013	Angiocardiogram	LMCA not shown again, Unknown	
16	20-NOV-2013	Angiocardiogram	RCA still with good results after PCI, Unknown	
17	02-AUG-2013	Aspiration bone marrow	No evidence of MDS, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
18	02-AUG-2013	Aspiration bone marrow	B12 and folic acid deficiencies also ruled out, Un	
19	06-AUG-2013	Aspiration bone marrow	Few megakaryocytes, Unknown	
20	06-AUG-2013	Aspiration bone marrow	Erythropoiesis forming megaloblasts, Unknown	
21	06-AUG-2013	Aspiration bone marrow	Blood present in the bone marrow, Unknown	
22	06-AUG-2013	Aspiration bone marrow	Differentiating granulocytopoiesis, Unknown	
23		Biopsy bone	Slight eosinophilia, unknown	
24		Biopsy bone	Slight increase in nucleated cells, unknown	
25	06-AUG-2013	Biopsy bone	Initial blasts forming, megaloblastic, Unknown	
26	06-AUG-2013	Biopsy bone	Granulocytopoiesis was differentiated, Unknown	
27	06-AUG-2013	Biopsy bone	at the expense of yellow marrow, Unknown	
28	06-AUG-2013	Biopsy bone	Erythropoiesis slightly impaired cell maturation,	
29	10-JUN-2015	Biopsy bone	Megakaryocytes presently without atypia, Unknown	
30	08-APR-2015	Blood alkaline phosphatase	189.00 (increased) IU/l	
31	02-JUN-2015	Blood cholesterol	253.00 (increased) mg/dl	
32	17-NOV-2013	Blood creatine phosphokinase	109, unknown	
33	17-NOV-2013	Blood creatine phosphokinase	101, unknown	
34	18-NOV-2013	Blood creatine phosphokinase	97, Unknown	
35	18-NOV-2013	Blood creatine phosphokinase	89, Unknown	
36	19-NOV-2013	Blood creatine phosphokinase	127, unknown	
37	20-NOV-2013	Blood creatine phosphokinase	115, Unknown	
38	01-JAN-2015	Blood creatine phosphokinase	63 IU/l	145 0
39	10-JUN-2015	Blood creatine phosphokinase	56 IU/l	145 0
40	12-JUN-2015	Blood creatine phosphokinase	63 IU/l	145 0
41	17-NOV-2013	Blood creatine phosphokinase MB	82, Unknown	
42	17-NOV-2013	Blood creatine phosphokinase MB	98, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
43	18-NOV-2013	Blood creatine phosphokinase MB	70, Unknown	
44	18-NOV-2013	Blood creatine phosphokinase MB	54, Unknown	
45	19-NOV-2013	Blood creatine phosphokinase MB	59, Unknown	
46	20-NOV-2013	Blood creatine phosphokinase MB	71, Unknown	
47		Blood creatinine	2.04 mg/dl	
48	04-SEP-2013	Blood creatinine	2.47 mg/dl	
49	25-MAR-2015	Blood creatinine	2.60 (increased) mg/dl	
50	08-APR-2015	Blood creatinine	2.80 (increased) mg/dl	
51	21-APR-2015	Blood creatinine	2.56 (increased) mg/dl	
52	07-MAY-2015	Blood creatinine	2.41 (increased) mg/dl	
53	18-MAY-2015	Blood creatinine	2.44 (increased) mg/dl	
54	02-JUN-2015	Blood creatinine	3.16 (increased) mg/dl	
55	10-AUG-2013	Blood culture	Negative, Unknown	
56	06-AUG-2013	Blood iron	Normal iron content of the marrow reticulum, Unkno	
57	06-AUG-2013	Blood iron	Ring sideroblasts were not present, Unknown	
58	01-JAN-2015	Blood lactate dehydrogenase	121 IU/l	247 110
59	10-JUN-2015	Blood lactate dehydrogenase	126 IU/l	247 110
60	12-JUN-2015	Blood lactate dehydrogenase	135 IU/l	247 110
61	07-MAY-2015	Blood potassium	3.40 (decreased) mmol/l	
62	18-MAY-2015	Blood potassium	3.40 (decreased) mmol/l	
63	10-JUN-2015	Blood pressure measurement	125/81 mmHg	
64	06-AUG-2013	Blood smear test	Erythrocytes slightly enlarged, Unknown	
65	02-JUN-2015	Blood triglycerides	351.00 (increased) mg/dl	
66	25-MAR-2015	Blood urea	102.00 (increased) mg/dl	
67	08-APR-2015	Blood urea	97.00 (increased) mg/dl	
68	21-APR-2015	Blood urea	90.00 (increased) mg/dl	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
69	07-MAY-2015	Blood urea	112.00 (increased) mg/dl	
70	18-MAY-2015	Blood urea	124.00 (increased) mg/dl	
71	02-JUN-2015	Blood urea	141.00 (increased) mg/dl	
72	25-MAR-2015	Blood uric acid	8.37 (increased) mg/dl	
73	08-APR-2015	Blood uric acid	9.43 (increased) mg/dl	
74	21-APR-2015	Blood uric acid	8.97 (increased) mg/dl	
75	07-MAY-2015	Blood uric acid	8.59 (increased) mg/dl	
76	18-MAY-2015	Blood uric acid	8.29 (increased) mg/dl	
77	02-JUN-2015	Blood uric acid	9.16 (increased) mg/dl	
78	10-AUG-2013	Breath sounds	Eupnoea, vesicular breath sounds, Unknown	
79	17-NOV-2013	Breath sounds	Dyspnoea, tachypnoea, coarse bubbly crepitations	
80	17-NOV-2013	Breath sounds	Ubiquitous spasticity, Unknown	
81	10-JUN-2015	Breath sounds	Vesicular on both sides, Unknown	
82	04-SEP-2013	C-reactive protein	2.47 mg/l	6.0 0.0
83	01-JAN-2015	C-reactive protein	57.48 mg/l	6.0 0.0
84	25-MAR-2015	C-reactive protein	60.00 (increased) mg/l	6.0 0.0
85	08-APR-2015	C-reactive protein	18.00 (increased) mg/l	6.0 0.0
86	21-APR-2015	C-reactive protein	20.00 (increased) mg/l	6.0 0.0
87	07-MAY-2015	C-reactive protein	7.00 (increased) mg/l	6.0 0.0
88	02-JUN-2015	C-reactive protein	6.00 (increased) mg/l	6.0 0.0
89	10-JUN-2015	C-reactive protein	13.65 mg/l	6.0 0.0
90	12-JUN-2015	C-reactive protein	71.69 mg/l	6.0 0.0
91		Colonoscopy	Normal, Unknown	
92		Computerised tomogram	No other evidence of secondary cause of dementia,	
93		Computerised tomogram abdomen	Normal, Unkonwn	
94		Computerised tomogram abdomen		

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
95	10-JUN-2015	Computerised tomogram abdomen		
96	26-AUG-2013	Computerised tomogram head	With moderate signs of vascular encephalopathy, U	
97	26-AUG-2013	Computerised tomogram head	No evidence of intracerebral haemorrhage, Unknown	
98	26-AUG-2013	Computerised tomogram head	No disturbance to circulation of CSF, Unknown	
99	26-AUG-2013	Computerised tomogram head	Moderate regression marked in white matter, Unknow	
100	26-AUG-2013	Computerised tomogram head	No evidence of new or prev. ischaemic areas, Unkno	
101	09-APR-2015	Computerised tomogram head	Not reported, unknown	
102	10-JUN-2015	Computerised tomogram head	Status unchanged. Advanced microangiopathic, Unkno	
103	10-JUN-2015	Computerised tomogram head	evidence of intracranial bleeding., unknown	
104	10-JUN-2015	Computerised tomogram head	changes. Slight generalised atrophy WITH NO, Unkno	
105	10-JUN-2015	Computerised tomogram head	No distinctive new signs of ischaemia, Unknown	
106	11-JUN-2015	Computerised tomogram head	Clinical posterior infarction with rightside side,	
107	11-JUN-2015	Computerised tomogram head	Still no evidence of intracerebral bleeding, Unkno	
108	11-JUN-2015	Computerised tomogram head	the ischaemia is attributed to the posterior, Unk	
109	11-JUN-2015	Computerised tomogram head	cerebral artery, Unknown	
110	11-JUN-2015	Computerised tomogram head	homonymous hemiparesis, Unknown	
111	11-JUN-2015	Computerised tomogram head	temporal lobe reaching as far as the basal gangli	
112	11-JUN-2015	Computerised tomogram head	No significant pressure components. The area of, U	
113		Computerised tomogram thorax	Normal, Unknown	
114	06-AUG-2013	Cytology	65 % granulocytes, 30 % lymphocytes 5 % monocytes,	
115	06-AUG-2013	Cytology	No eosinophils or basophiles, Unknown	
116		Diagnostic procedure	5 points, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
117		Echocardiogram	V.cava collaptic, slight pleu. effusion both side	
118		Echocardiogram	LV dyskinesia, EF still normal, Unknown	
119		Echocardiogram	LA slightly enlarged, suspected post. hypokinesia,	
120		Echocardiogram	No PE, no congestion on either kidney, Unknown	
121		Echocardiogram	Slight AI, MI, TI, RSVP 40 mmHg, unknown	
122		Echocardiogram	LV normal size, LV hyperthrophy, Unknown	
123	12-JUN-2015	Echocardiogram	No localised valves with FDE, Unknown	
124	12-JUN-2015	Echocardiogram	no hypertrophy. Normal LV function, Unknown	
125	12-JUN-2015	Echocardiogram	Left side heart cavities not enlarged, Unknown	
126	12-JUN-2015	Echocardiogram	slight aortic valve reflux with strong sclerosis	
127	12-JUN-2015	Echocardiogram	with PAH, Unknown	
128	12-JUN-2015	Echocardiogram	Right side heart cavities somewhat enlarged	
129		Electrocardiogram	during internal rhythm, Unknown	
130		Electrocardiogram	Heart axis could not be determined, unknown	
131		Electrocardiogram	Repolarisation disturbances cause by block, unknow	
132		Electrocardiogram	and VVI stimulation, Unknown	
133		Electrocardiogram	Alteration between internal rhythm(SR), Unknown	
134		Electrocardiogram	With incomplete left ant. hemiblock, unknown	
135		Electrocardiogram	Heart axis was left biased, unknown	
136		Electrocardiogram	Change SM-VVI with rhythm at 79/min, Unknown	
137		Electrocardiogram	Complete RBBB, LAH, Unknown	
138		Electrocardiogram	Complete RBBB, unknown	
139	17-NOV-2013	Electrocardiogram	72/min, Unknown	
140	10-JUN-2015	Electrocardiogram	Pacemaler actions, left axis deviation, Unknown	
141		Endoscopy upper gastrointestinal	Normal, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		tract		
142	08-APR-2015	Gamma-glutamyltransferase	64.00 (increased) IU/l	
143		Gastrointestinal examination		
144	10-AUG-2013	Gastrointestinal examination	Regular peristaltic sounds, no resistance palpable	
145	10-AUG-2013	Gastrointestinal examination	No tenderness on palpitation, no muscular guarding	
146	17-NOV-2013	Gastrointestinal examination	Regular peristaltic sounds, no resistance palpabl	
147	17-NOV-2013	Gastrointestinal examination	No tenderness on palpitation, no muscular guardin	
148	22-NOV-2013	Gastrointestinal examination	22Nov2013	
149	10-JUN-2015	Gastrointestinal examination	No pathological findings. Unknown	
150	04-SEP-2013	Glomerular filtration rate	20 ml/min	60
151	25-MAR-2015	Glomerular filtration rate	19.00 (decreased)	
152	08-APR-2015	Glomerular filtration rate	17.00 (decreased)	
153	21-APR-2015	Glomerular filtration rate	19.00 (decreased)	
154	07-MAY-2015	Glomerular filtration rate	20.00 (decreased)	
155	18-MAY-2015	Glomerular filtration rate	20.00 (decreased)	
156	02-JUN-2015	Glomerular filtration rate	15.00 (decreased)	
157	18-AUG-2015	Glomerular filtration rate	15 ml/min	60
158	07-AUG-2013	Haematocrit	28.40 %	
159	07-AUG-2013	Haematocrit	27.9 %	
160	04-OCT-2013	Haematocrit	26.10 %	
161	04-OCT-2013	Haematocrit	26.9 %	
162	01-NOV-2013	Haematocrit	26.8 %	
163	01-NOV-2013	Haematocrit	26.20 %	
164	17-NOV-2013	Haematocrit	31.5,Unknown	
165	18-NOV-2013	Haematocrit		47 35

Mfr. Control Number: 2126673

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
166	18-NOV-2013	Haematocrit	29.0, Unknown	
167	18-NOV-2013	Haematocrit	27.3,Unknown	
168	19-NOV-2013	Haematocrit	25.8,Unknown	
169	19-NOV-2013	Haematocrit		47 35
170	20-NOV-2013	Haematocrit		47 35
171	20-NOV-2013	Haematocrit	28.3, Unknown	
172	22-NOV-2013	Haematocrit	26.0, Unknown	
173	22-NOV-2013	Haematocrit		47 35
174	23-NOV-2013	Haematocrit		47 35
175	23-NOV-2013	Haematocrit	27.0, Unknown	
176	25-NOV-2013	Haematocrit		47 35
177	25-NOV-2013	Haematocrit	25.9, Unknown	
178	27-NOV-2013	Haematocrit	27.3, Unknown	
179	27-NOV-2013	Haematocrit		47 35
180	01-JAN-2015	Haematocrit	24.6, FL	47 35
181	25-MAR-2015	Haematocrit	21.40 (decreased) %	
182	08-APR-2015	Haematocrit	21.20 (decreased) %	
183	21-APR-2015	Haematocrit	26.50 (decreased) %	
184	07-MAY-2015	Haematocrit	27.70 (decreased) %	
185	18-MAY-2015	Haematocrit	27.90 (decreased) %	
186	02-JUN-2015	Haematocrit	27.00 (decreased) %	
187	10-JUN-2015	Haematocrit	23.7, FL	47 35
188	12-JUN-2015	Haematocrit	26.0, FL	47 35
189	12-JUN-2015	Haematocrit	21.6, FL	47 35
190	16-AUG-2015	Haematocrit	26.5 fL	47 35
191	18-AUG-2015	Haematocrit	23 %	46 36

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
192		Haemoglobin	3.5 mg/dl	
193	07-AUG-2013	Haemoglobin	9.10 g/dl	
194	04-OCT-2013	Haemoglobin	8.50 g/dl	
195	01-NOV-2013	Haemoglobin	8.50 g/dl	
196	17-NOV-2013	Haemoglobin	10.2, Unknown	
197	18-NOV-2013	Haemoglobin	9.4, Unknown	
198	18-NOV-2013	Haemoglobin	8.7, Unknown	
199	19-NOV-2013	Haemoglobin	8.1, Unknown	
200	20-NOV-2013	Haemoglobin	3.1, Unknown	
201	22-NOV-2013	Haemoglobin	8.2, unknown	
202	23-NOV-2013	Haemoglobin	8.5, unknown	
203	25-NOV-2013	Haemoglobin	8.2, Unknown	
204	27-NOV-2013	Haemoglobin	8.7, Unknown	
205	01-JAN-2015	Haemoglobin	7.8 g/dl	16.9 10.9
206	25-MAR-2015	Haemoglobin	6.80 (decreased) g/dl	
207	08-APR-2015	Haemoglobin	6.70 (decreased) g/dl	
208	21-APR-2015	Haemoglobin	8.30 (decreased) g/dl	
209	07-MAY-2015	Haemoglobin	8.70 (decreased) g/dl	
210	18-MAY-2015	Haemoglobin	9.0 under main dose no. 2 g/dl	
211	28-MAY-2015	Haemoglobin	9.0 mg/dl	
212	02-JUN-2015	Haemoglobin	8.80 (decreased) g/dl	
213	02-JUN-2015	Haemoglobin	8.8 mg/dl	
214	07-JUN-2015	Haemoglobin	8.8 under main dose no. 1 g/dl	
215	10-JUN-2015	Haemoglobin	7.8 g/dl	16.9 10.9
216	12-JUN-2015	Haemoglobin	8.2 g/dl	16.9 10.9
217	12-JUN-2015	Haemoglobin	8.5 g/dl	16.9 10.9

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
218	18-AUG-2015	Haemoglobin	7.5 g/dl	16 12
219	25-MAR-2015	Haptoglobin	257.00 (increased) mg/dl	
220	10-JUN-2015	Heart rate	70 /min, Unknown	
221	10-JUN-2015	Heart rate	65/ min, Unknown	
222	10-AUG-2013	Heart sounds	Rhythmic, heart tones pure, Unknown	
223	17-NOV-2013	Heart sounds	Rhythmic, heart tones pure, Unknown	
224	17-NOV-2013	Heart sounds		
225	17-NOV-2013	Heart sounds		
226	17-NOV-2013	Heart sounds		
227	17-NOV-2013	Heart sounds		
228	17-NOV-2013	Heart sounds		
229	17-NOV-2013	Heart sounds		
230	17-NOV-2013	Heart sounds		
231	18-NOV-2013	Heart sounds	LMCA not shown again, Unknown	
232	18-NOV-2013	Heart sounds		
233	18-NOV-2013	Heart sounds		
234	10-JUN-2015	Heart sounds	Normal and arrhythmic, Unknown	
235		Immunohistochemistry	Plasma were arranged perivascularly, Unknown	
236		Immunohistochemistry	No evidence of continuous CD20-expressing-B-cells	
237	06-AUG-2013	Immunohistochemistry	CD-34 expressing precursors cells not elevated	
238	06-AUG-2013	Immunohistochemistry	Count of CD138-labelled plasma between 5 - 6%	
239		Inflammatory marker test	Regressed, Unknown	
240		Inflammatory marker test	Increased, Unknown	
241	17-NOV-2013	International normalised ratio	1.00, Unknown	
242	18-NOV-2013	International normalised ratio	1.08, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
243	19-NOV-2013	International normalised ratio	1.10 , Unknown	
244	20-NOV-2013	International normalised ratio	1.01, Unknown	
245	22-NOV-2013	International normalised ratio	1.05, Unknown	
246	10-JUN-2015	International normalised ratio	21 seconds	33 22
247	10-JUN-2015	International normalised ratio	0.97, Unknown	1.24 1.0
248	25-MAR-2015	Mean cell haemoglobin	35.10 (increased) pg	
249	08-APR-2015	Mean cell haemoglobin	35.40 (increased) pg	
250	21-APR-2015	Mean cell haemoglobin	33.90 (increased) pg	
251	07-MAY-2015	Mean cell haemoglobin	34.10 (increased) pg	
252	18-MAY-2015	Mean cell haemoglobin	35.30 (increased) pg	
253	02-JUN-2015	Mean cell haemoglobin	36.10 (increased) pg	
254	25-MAR-2015	Mean cell haemoglobin concentration	31.80 (decreased) g/dl	
255	08-APR-2015	Mean cell haemoglobin concentration	31.60 (decreased) g/dl	
256	21-APR-2015	Mean cell haemoglobin concentration	31.30 (decreased) g/dl	
257	07-MAY-2015	Mean cell haemoglobin concentration	31.40 (decreased) g/dl	
258	18-MAY-2015	Mean cell haemoglobin concentration	32.20 (decreased) g/dl	
259	02-JUN-2015	Mean cell haemoglobin concentration	32.60 (decreased) g/dl	
260	25-MAR-2015	Mean cell volume	110.00 fl (increased)	
261	08-APR-2015	Mean cell volume	112.00 fl (increased)	
262	21-APR-2015	Mean cell volume	108.00 fl (increased)	
263	07-MAY-2015	Mean cell volume	109.00 fl (increased)	
264	18-MAY-2015	Mean cell volume	109.00 fl (increased)	
265	02-JUN-2015	Mean cell volume	111.00 fl (increased)	
266		Mini mental status examination	20 points, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
267	10-AUG-2013	Neurological examination	Normal, Unknown	
268	17-NOV-2013	Neurological examination	Normal findings, Unknown	
269	10-JUN-2015	Neurological examination	Patient awake, orientation somewhat unfocused	
270	10-JUN-2015	Neurological examination	cardioembolic posterior medial insular, Unknown	
271	10-JUN-2015	Neurological examination	in terms of age, with reduced speech comprehensio	
272	10-JUN-2015	Neurological examination	left hemispheric, Unknown	
273	11-JUN-2015	Neurological examination	homonymous hemiparesis	
274	11-JUN-2015	Neurological examination	Clinical posterior infarction with rightside, Unkn	
275	10-JUN-2015	Ophthalmological examination	Isochoric, Unknown	
276	10-JUN-2015	Oxygen saturation	97 %	
277	10-AUG-2013	Physical examination	Impaired/delayed cognitive ability, Unknown	
278	10-AUG-2013	Physical examination	Dehydrated, oedema in both legs, Unknown	
279	10-AUG-2013	Physical examination	Foot pulse cannot be felt on either side, Unknown	
280	10-AUG-2013	Physical examination	Reduce general health, adipose nutritional status	
281	17-NOV-2013	Physical examination	Adipose nutritional status, Unknown	
282	17-NOV-2013	Physical examination	Severely deteriorated general health, Unknown	
283	17-NOV-2013	Physical examination	Leg oedema on both sides, Unknown	
284	10-JUN-2015	Physical examination	Right hemiparesis accentuated in right am, Unknown	
285	10-JUN-2015	Physical examination	Oriented in space but not in time (1955), Unknown	
286	10-JUN-2015	Physical examination	Oriented about self, Unknown	
287	17-NOV-2013	Platelet count	264, unknown	
288	18-NOV-2013	Platelet count	235, Unknown	
289	18-NOV-2013	Platelet count	212, Unknown	
290	19-NOV-2013	Platelet count	209, unknown	
291	20-NOV-2013	Platelet count	216, unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
292	22-NOV-2013	Platelet count	209, unknown	
293	22-NOV-2013	Platelet count	218, Unknown	
294	23-NOV-2013	Platelet count	220, Unknown	
295	25-NOV-2013	Platelet count	248, Unknown	
296	27-NOV-2013	Platelet count	269, Unknown	
297	01-JAN-2015	Platelet count	185 10S3/mcL, Unknown	409 139
298	10-JUN-2015	Platelet count	266 10S3/mcL, unknown	409 139
299	12-JUN-2015	Platelet count	205 10S3/mcL, Unknown	409 139
300	18-AUG-2015	Platelet count	232 Tsd/uL, Unknown	400 150
301	17-NOV-2013	Prothrombin time	105, Unknown	
302	18-NOV-2013	Prothrombin time	90, Unknown	
303	19-NOV-2013	Prothrombin time	88, Unknown	
304	20-NOV-2013	Prothrombin time	100, Unknown	
305	22-NOV-2013	Prothrombin time	94, Unknown	
306	10-JUN-2015	Prothrombin time	107 %	130 70
307	10-AUG-2013	Rectal examination	Normal, Unknown	
308	07-AUG-2013	Red blood cell count	2.37 Mill/mcl, Unknown	
309	04-OCT-2013	Red blood cell count	2.25 Mill/mcl, Unknown	
310	01-NOV-2013	Red blood cell count	2.30 Mill/mcl, unknown	
311	17-NOV-2013	Red blood cell count	2.37 Mill/mcl, Unknown	5.1 4.1
312	17-NOV-2013	Red blood cell count	2.74, Unknown	5.1 4.1
313	18-NOV-2013	Red blood cell count	2.35, Unknown	5.1 4.1
314	18-NOV-2013	Red blood cell count	2.48, Unknown	5.1 4.1
315	18-NOV-2013	Red blood cell count		5.1 4.1
316	20-NOV-2013	Red blood cell count	2.36, Unknown	5.1 4.1
317	22-NOV-2013	Red blood cell count	2.01, Unknown	5.1 4.1

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
318	22-NOV-2013	Red blood cell count	2.22, Unknown	5.1 4.1
319	23-NOV-2013	Red blood cell count	2.29, Unknown	5.1 4.1
320	25-NOV-2013	Red blood cell count	2.25, Unknown	5.1 4.1
321	27-NOV-2013	Red blood cell count	2.38, Unknown	5.1 4.1
322	01-JAN-2015	Red blood cell count	2.31 10S3/mcL, unknown	5.1 4.1
323	25-MAR-2015	Red blood cell count	1.94 mio/ul (decreased)	
324	08-APR-2015	Red blood cell count	1.89 mio/ul (decreased)	
325	21-APR-2015	Red blood cell count	2.45 mio/ul (decreased)	
326	07-MAY-2015	Red blood cell count	2.55 mio/ul (decreased)	
327	18-MAY-2015	Red blood cell count	2.55 mio/ul (decreased)	
328	02-JUN-2015	Red blood cell count	2.44 mio/ul (decreased)	
329	10-JUN-2015	Red blood cell count	2.09 10S3/mcL, Unknown	5.1 4.1
330	12-JUN-2015	Red blood cell count	2.2 10S3/mcL, Unknown	5.1 4.1
331	12-JUN-2015	Red blood cell count	2.3 10S3/mcL, Unknown	5.1 4.1
332	18-AUG-2015	Red blood cell count	1.95 Mio/uL, Unknown	5.2 3.9
333	10-JUN-2015	Red blood cell sedimentation rate	64 mm/h, Unknown	10 2
334	10-JUN-2015	Respiratory rate	13/ min, Unknown	
335	25-MAR-2015	Reticulocyte count	18.00 (increased)	
336	08-APR-2015	Reticulocyte count	22.00 (increased)	
337	21-APR-2015	Reticulocyte count	17.00 (increased)	
338	07-MAY-2015	Reticulocyte count	18.00 (increased)	
339	18-MAY-2015	Reticulocyte count	17.00 (increased)	
340	08-APR-2015	Serum ferritin	591.00 ug/l (increased)	
341	17-NOV-2013	Troponin T	48.2, Unknown	
342	18-NOV-2013	Troponin T	59.8 Unknown	
343		Ultrasound Doppler	Not reported, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
344	10-JUN-2015	Ultrasound Doppler	of a relevant stenosis Flow: 160-180 cm/s, Unknown	
345	10-JUN-2015	Ultrasound Doppler	Left: narrowing of the lumen, no evidence	
346	10-JUN-2015	Ultrasound Doppler	lumen of the bulbs, Unknown	
347	10-JUN-2015	Ultrasound Doppler	Right: weaker findings, no flow acceleration	
348	10-JUN-2015	Ultrasound Doppler	Both sides calcified, plaque in the, Unknown	
349	13-JUN-2015	Urine analysis	urobilinogen normal, bilirubin negative,blood ++	
350	13-JUN-2015	Urine analysis	glucose normal, ketone negative, Unknown	
351	13-JUN-2015	Urine analysis	Leukocytes+++, nitrite positive, pH 5 , protein+	
352		X-ray of pelvis and hip	Not reported, Unknown	

13. Relevant Tests

Abdomen (unknown date): No tenderness on palpitation, no muscular guarding, Unknown
Abdomen (unknown date): Regular peristaltic sounds, no resistance palpable, Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	167 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	02-MAY-2012 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	4000 E, thrice weekly; Subcutaneous	Renal anemia (Nephrogenic anaemia)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	12000 IU, 3 x weekly; Unknown	Renal anemia (Nephrogenic anaemia)	07-JUN-2015 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #4	12000 IU, 3 x weekly; Unknown	Renal anemia (Nephrogenic anaemia)	18-MAY-2015 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX) ; 15-OCT-2009 / Unknown

#4) CALCIUM-D3 (CALCIUM CARBONATE, COLECALCIFEROL) Tablet ; 03-MAY-2009 / Unknown

#6) NOVALGIN /00169801/ (CAFFEINE, PARACETAMOL, PROPYPHENAZONE) ; 03-MAY-2009 / Unknown

#7) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; 03-MAY-2009 / Unknown

#8) RESOLOR (PRUCALOPRIDE SUCCINATE) Coated tablet ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#9) TARGIN (NALOXONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE) ; 19-MAR-2009 / Unknown

#10) TORASEMID (TORASEMIDE) Tablet ; 05-NOV-2014 / Unknown

#11) ALENDRONAT (ALENDRONATE SODIUM) ; 11-JAN-2007 / Unknown

#12) ASA (ACETYLSALICYLIC ACID) Tablet ; 19-MAR-2014 / Unknown

#13) CLOPIDOGREL HYDROCHLORIDE (CLOPIDOGREL HYDROCHLORIDE) ; 19-MAR-2014 / Unknown

#14) LACTULOSE (LACTULOSE) ; 07-AUG-2013 / Unknown

#15) MACROGOL (MACROGOL) Powder for injection ; 19-MAR-2009 / Unknown

#16) METAMIZOLE /06276704/ (METAMIZOLE SODIUM) Tablet ; Unknown

#17) ABZ (ALBENDAZOLE) Tablet ; Unknown

#18) ABZ (ALBENDAZOLE) Powder for injection ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Cerebrosclerosis (Cerebrosclerosis);
Unknown to Ongoing	Relevant Med History	Chronic interstitial nephritis (Tubulointerstitial nephritis);
Unknown to Ongoing	Relevant Med History	Kidney disorder (Renal disorder);
Unknown to Ongoing	Relevant Med History dementia of mixed type	Dementia (Dementia);
Unknown to Ongoing	Relevant Med History	General physical health deterioration (General physical health deterioration);
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Exsiccosis (Dehydration);
DEC-2008 to Ongoing	Relevant Med History	Hyperchromic anaemia (Hyperchromic anaemia);
DEC-2008 to Ongoing	Relevant Med History	Macrocytic anaemia (Anaemia macrocytic);
Unknown to Ongoing	Relevant Med History	Hypertensive heart disease (Hypertensive heart disease);
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Hypertriglyceridaemia (Hypertriglyceridaemia);
Unknown to Ongoing	Relevant Med History	Hypertriglyceridemia (Hypertriglyceridaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Liver damage (Liver injury);
Unknown to Ongoing	Relevant Med History	Appetite lost (Decreased appetite);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Falling (Fall);
Unknown to Ongoing	Relevant Med History	Nephroangiosclerosis (Nephroangiosclerosis);
Unknown to Ongoing	Relevant Med History	Varices oesophageal (Varices oesophageal);
AUG-2006 to Ongoing	Relevant Med History Aug 2006	Osteoporosis (Osteoporosis);
Unknown to Ongoing	Relevant Med History	Psoriasis (Psoriasis);
Unknown to Ongoing	Relevant Med History gastrointestinal disease described as recurrent gastritis	Gastritis (Gastritis);
02-SEP-2005 to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Colonic diverticulosis (Diverticulum intestinal);
Unknown to Ongoing	Relevant Med History	Lumbar disc herniation (Intervertebral disc protrusion);
Unknown to Ongoing	Relevant Med History	Urinary tract infection (Urinary tract infection);
Unknown to Ongoing	Relevant Med History	Mobility decreased (Mobility decreased);
31-JUL-2013 to Unknown	Relevant Med History on 31Jul2013 with no evidence of MDS	Bone marrow aspiration (Aspiration bone marrow);
Unknown	Relevant Med History	Cholecystectomy (Cholecystectomy);
Unknown	Relevant Med History of MWK 12, LWK 1, and 2	Compression fracture (Compression fracture);
Unknown	Relevant Med History	Gravida I (Primigravida);
Unknown	Relevant Med History	Parity 1 (Primiparous);
Unknown	Relevant Med History	Hiatus hernia (Hiatus hernia);
2008 to Unknown	Relevant Med History	Incisional hernia (Incisional hernia);
27-OCT-2009 to 07-APR-2010	Past Drug Event in 2009/2010, 167 IU/kg/week, dose 75-120 and hemoglobin 8.5 - 9.2 g/dl, there was a change of ESA, did not experience any thromboembolic event during treatment with of any other ESA; update (01Jul2019): no AE occcurred under MIRCERA	Mircera (MIRCERA); Drug Reaction: Drug ineffective (Drug ineffective)
Unknown	Relevant Med History Jan-2008	Adhesiolysis (Adhesiolysis);
Unknown	Relevant Med History 23-Sep-2010 to 26-Oct-2010	MRSA wound infection (Wound infection staphylococcal);
Unknown	Relevant Med History LWK 4/5	Osteoporotic fracture (Osteoporotic fracture);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
JUL-2007 to Unknown	Relevant Med History	Pacemaker insertion (cardiac) (Cardiac pacemaker insertion);
JUL-2007 to Unknown	Relevant Med History	Sick sinus syndrome (Sinus node dysfunction);
MAY-2011 to Unknown	Relevant Med History	Pelvic fracture (Pelvic fracture);
MAY-2006 to Unknown	Relevant Med History	Percutaneous transluminal angioplasty (Angioplasty);
12-JUL-2006 to Unknown	Relevant Med History on the right on 12-Jul-2006	Shoulder prosthesis user (Joint prosthesis user);
Unknown	Relevant Med History	Gastrointestinal fistula repair (Gastrointestinal fistula repair);
Unknown	Relevant Med History	Vertebral body hemangioma (Haemangioma of bone);
04-AUG-2006 to Unknown	Relevant Med History	Vertebroplasty (Vertebroplasty);
01-SEP-2005 to Ongoing	Relevant Med History	Hypertension arterial (Hypertension);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Cerebrovascular disorder (Cerebrovascular disorder);
31-JUL-2013 to Unknown	Relevant Med History sintering; 31-Jul-2013	Fracture of spine (Spinal fracture);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
04-AUG-2006 to Ongoing	Relevant Med History	Immobile (Immobile);
Unknown	Relevant Med History	Chronic pain (Pain);
Unknown to Ongoing	Relevant Med History BMI: 29.4	Obesity (Obesity);
MAY-2006 to Ongoing	Relevant Med History affecting pelvic arteries on the right	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease);
01-DEC-2008 to Ongoing	Relevant Med History Dec 2008	Polymyalgia (Myalgia);
01-SEP-2005 to Ongoing	Relevant Med History Sep 2005, controlled by HbA 1c 4.4 %	Type II diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Wheelchair user (Wheelchair user);
21-APR-2010 to 15-MAR-2012	Past Drug Event dose 50-150 and hemoglobin 8.4 - 12.2 g/dl, prior to starting Retacrit	ARANESP (ARANESP);
31-JUL-2013 to Ongoing	Relevant Med History sintering fracture spine	Trauma (Injury);
Unknown	Relevant Med History vessel anomaly	Peripheral arterial disease (Peripheral arterial occlusive disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	GERMANY	19	MAY	1940	73 Years	Female	108.90 kg	23	NOV	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Intervention Required
Macula infarction left eye [Retinal infarction]
NSTEMi [Acute myocardial infarction]
Sudden cardiac death at home [Sudden cardiac death]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of macula infarction
left eye and NSTEMi.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 11-JUL-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 U (Mo (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 08-AUG-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX)
#2) JATROSOM /00042001/ (TRANYLCYPROMINE SULFATE, TRIFLUOPE
#3) KALINOR /00031402/ (POTASSIUM CHLORIDE) ; 02-APR-2009 / Unknown
#4) NOVAMINSULFON (METAMIZOLE SODIUM) ; 09-FEB-2011 / Unknown
#5) ALLOPURINOL (ALLOPURINOL) ; 09-FEB-2011 / Unknown
#6) ASS (ACETYLSALICYLIC ACID) ; 08-AUG-2012 / Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History 01-Mar-2008; chronic gastrointestinal disease	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2131955

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-AUG-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case from an investigator (reference: Ge-432-0015) describes a 73-year-old female patient (weight: 108.9 kg and height: 175 cm) who received Retacrit (epoetin zeta, subcutaneous, three times weekly, batch number unknown; dose not reported) for renal anemia from 08-Aug-2012. Medical history included obesity with BMI of 35.6, hyperuricemia, abuse of diuretics, hyperlipidemia, ischemic heart disease, transient ischemic attack on 23-Nov-2013, hypertension; and chronic gastrointestinal disease on 01-Mar-2008 which included peptic ulcers, GI-bleeding, diverticulitis, and adenomas. The patient was not at anytime exposed to any other erythropoietin-stimulating agent (ESA). Concomitant medications included bisoprolol (2.5 mg, once a day) for hypertension, torasemid (150 mg, three times a day) for renal insufficiency, allopurinol (150 mg, once a day) for hyperuricemia, Jatrosom (10 mg, once a day) for nerves, clopidogrel (75 mg, once a day) for coronary heart disease, ASS (100 mg, once a day) for coronary heart disease, pravastatin (40 mg, once a day) for hyperlipidemia, Kalinor tbl. (2-3times/day) for hypokalemia, Novaminsulfon sol. (as needed, dose not reported) for pain, and Ferrlecit (625 mg, every fortnight) for anemia; all routes of administration not reported. On 08-Aug-2012, the patient started treatment with epoetin zeta. The patient received the last dose of epoetin zeta on 22-Nov-2013 prior to the adverse events. On 23-Nov-2013, the patient experienced macula infarction left eye described as blindness left eye. No treatment was given for the adverse event. On 03-Dec-2013, the patient developed NSTEMi with angina pectoris and was hospitalised on the same day. Coronagraphy was perfomed (results not provided). Treatment for the event of NSTEMi included application of stents and PTCA. On 23-Dec-2013, the patient's laboratory tests included HB of 11.10 g/dl, HKT 32.90 % and ERY of 3.42 Mill/mcl; normal values were not reported. Action taken with suspect epoetin zeta was not reported. At the time of the report, outcome of macula infarction left eye was not recovered; while persistent/significant disability for the event of NSTEMi with event end date reported as 18-Dec-2013. On the same day of 18-Dec-2013, the patient was discharged from the hospital. On 06-Jan-2014, additional laboratory tests included HB of 9.90 g/dl, HKT 30.70 % and ERY of 3.15 Mill/mcl. The reporter's causality assessment for the events of macula infarction left eye and NSTEMi in relation to epoetin zeta was unlikely. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered. 20-Jan-2014: English translation of the German discharge letter was received. Follow up report was created to reflect additional information regarding suspect drug, medical history, diagnostics, laboratory tests and adverse events. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: dosage administered. The patient received Retacrit at a dose of 3 x 2000 U/week (Mo We Fr). Additional medical history included NSTEMI on 09/09, PTCA and tract stent implant of the RCA on 09/09, PTCA BMS of the prox. RCA on 05/08, PTCA 2x DES of the prox. LAD on 04/08, AV block 1, chronic kidney failure according to KDOQI stage IV, benzodiazepine and alcohol dependency, peptic ulcer on 03/08, TIA on 12/11, and cardiovascular risk factors which included positive family history, and adiposity. The patient had an ongoing symptoms of AP for one week; noted elevated trop t level with HA, patient consequently presented to the emergency physician. The patient had already received ASA and heparin from the emergency physician. The patient exhibited no symptoms in the outpatient clinic. However, she reported a macular infarction with loss of sight on the left 10 days earlier. Since then she has been nervous and agitated. The physical examination of the patient showed reduced overall condition and with adipose nutritional status, conscious and oriented, no cyanosis, no dyspnoea at rest, no icterus. Initial pressure was 181/86 mmHg (normal values not reported), over the course of examination 150/55 mmHg, HR 73/min, regular oxygen saturation 100%, temperature 36.4 degrees C, respiratory rate 20. Lungs exam showed vesicular breath, sounds in all fields, no crepitations. Heart tones pure and rhythmic, no heart sounds typical of a defect. Abdomen was soft, no pain on palpitation, no side pain, normal borborygmus, no resistances. Extremitities with no lower leg oedema. Neurology exam showed no focal neurological deficits. No significant pathological findings through the rest of the examination. On 03-Dec-2013, ECG revealed SR, 72/min, vertical heart axis, AV block 1, QTC 477 msec, complete right bundle branch block with repolarisation disturbances. On the same day, laboratory tests included creatinine 3.2 mg/dl, urea 94.9 mg/dl, Hb 10.9 g/l (normal values not reported), and remaining blood levels within normal range. On the same day of 03-Dec-2013, the patient was admitted as an inpatient as a result of suspected ACS. The hs troponin T was elevated at 79-80pg/ml , against the background of chronic kidney failure according to KDOQI IV, formal NSTEMI. Because of the symptoms and known coronary artery disease, after flushing, invasive diagnostics (cardiac catheter examination)were carried out on 11-Dec-2013. The invasive diagnostics revealed 3-vessel coronary artery disease. Hence a PTCA with 4x DE stent implant of the prox. central and distal RCA was performed. The post-interventional follow-up proved to be without complication but there was a remaining high-grade stenosis of the LCX. It was also reported that the patient had mild-grade restricted left ventricular function. There was no indication of aneurysms, fistulae or significant haematoma at the puncture site. Recommendation was dual thrombocyte aggregation inhibition with ASA and Brilique for 12 months. Subsequently, sole use of 100 mg ASA daily should suffice. For residual stenosis of the LCX, re-intervention in 8 weeks depending on the retention parameters was suggested. It was also reported that the patient had satisfactory result in connection with PTCA and DE stent implant of the LAD 05/2012 and PTCa and stent implant of the Ramus intermedius 2012 and PTCA/de stent implant of the prox RCA in association with in-stent restenosis and PTCA of the LCX. Based on the kidney failure and increased administration of contrast medium during implant of stents, the kidneys were flushed again. Ramipril was suspended. There was stable MDRD-GFR of 13ml/min/1.73 m^2 and a urea level approximately 110mg/dl upon discharge. It was requested that retention parameters were monitored and if necessary use of Ramipril was resumed. The patient in good overall status was discharged on 18-Dec-2013 to the follow-up care of her general practitioner. Consistent adjustment of cardiovascular risk factors (target LDL less than 70 mg/dl; target BP less than 130/80 mmHg) was recommended. 06-Aug-2014: Additional information was received from the same reporter. Follow-up report was created to reflect new information regarding patient detail, medical history, suspect drug, and adverse event. Fatal sudden cardiac death at home was added as adverse event. The patient’s weight was also reported as 100 kg. The dose of Retacrit (epoetin zeta) during the week

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

of entry into the study was 60 IU/kg/week. Medical history also included interstitial nephritis which led to renal failure diagnosed on 22-Mar-1994. The patient was not on dialysis. On 11-Jul-2014, the patient experienced sudden cardiac death at home. It was not reported if an autopsy was performed. Treatment for the event and action taken with epoetin zeta were not applicable. The patient did not complete the study because her death. The reporter's causality assessment for the event of cardiac death at home in relation to epoetin zeta was not reported. Risk factor also included coronary heart disease. The risk factor NSTEMI was also reported as myocardial infarction.

Case Comment: Overall case causality: Possible Even if the events are more likely due to natural pathogenesis of infarction given the significant cardiovascular risk factors, consider also possible contributory effects from the suspect drug as it can theoretically increase the risk of thrombosis by increasing red blood cell concentration. - N. Gonzales (16 Jan 2014) Follow-up: No change in previous causality assessment. - N. Gonzales (28 Jan 2014) Follow-up: New reported event of sudden cardic death is also possibly related, as this could be a potential sequela of the previously reported myocardial infarction. - N. Gonzales (14 Aug 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Angiocardiogram	Not reported, Unknown	
2	03-DEC-2013	Blood creatinine	3.2 mg/dl	
3		Blood pressure measurement	181/86 mmHg	
4		Blood pressure measurement	150/55 mmHg	
5	03-DEC-2013	Blood test	Within normal range, Unknown	
6	03-DEC-2013	Blood urea	94.9 mg/dl	
7	18-DEC-2013	Blood urea	110 mg/dl	
8		Body temperature	36.4 degrees Centigrade	
9		Breath sounds	Vesicular breath, sounds in all fields, Unknown	
10		Breath sounds	No crepitations, Unknown	
11		Catheterisation cardiac	3-vessel coronary artery disease, Unknown	
12	03-DEC-2013	Electrocardiogram	With repolarisation disturbances, Unknown	
13	18-DEC-2013	Glomerular filtration rate	13ml/min/1.73m^2, Unknown	
14	23-DEC-2013	Haematocrit	32.90 %	
15	06-JAN-2014	Haematocrit	30.70 %	
16	03-DEC-2013	Haemoglobin	10.9 g/l	
17	23-DEC-2013	Haemoglobin	11.10 g/dl	
18	06-JAN-2014	Haemoglobin	11.10 g/dl	
19		Heart rate	73/min, Unknown	
20		Heart sounds	Heart tones pure and rhythmic, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
21		Heart sounds	No heart sounds typical of a defect, Unknown	
22		Neurological examination	No focal neurological deficits, Unknown	
23		Oxygen saturation	100 %	
24		Physical examination	Adipose nutrional status, Unknown	
25		Physical examination	Conscious and oriented, no cyanosis, Unknown	
26		Physical examination	No dyspnoea at rest, no icterus, Unknown	
27		Physical examination	Soft, no pain on palpitation, no side pain,Unknown	
28		Physical examination	No lower leg oedema, Unknown	
29		Physical examination	Normal borborygmus, no resistances, Unknown	
30		Physical examination	Reduced overall condition, Unknown	
31	23-DEC-2013	Red blood cell count	3.42 Mill/mcl, Unknown	
32	06-JAN-2014	Red blood cell count	3.15 Mill/mcl, Unknown	
33		Respiratory rate	20, Unknown	
34	03-DEC-2013	Troponin T	79-80, PG/ML	

13. Relevant Tests

ECG (03-Dec-2013): QTC 477 msec, complete right bundle branch block, SR, 72/min, vertical heart axis, AV block 1, Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	2000 U (Mo We Fr), Freq: 3 Week, Interval: 1; Subcutaneous	Renal anemia (Nephrogenic anaemia)	08-AUG-2012 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) FERRLECIT /00023541/ (FERRIC SODIUM GLUCONATE COMPLEX) ; 08-AUG-2012 / Unknown

#2) JATROSOM /00042001/ (TRANYLCYPROMINE SULFATE, TRIFLUOPERAZINE HYDROCHLORIDE) ; 07-APR-2009 / Unknown

#7) BISOPROLOL (BISOPROLOL) ; 27-FEB-2012 / Unknown

#8) CLOPIDOGREL (CLOPIDOGREL) ; 27-FEB-2012 / Unknown

#9) PRAVASTATIN (PRAVASTATIN) ; 27-FEB-2012 / Unknown

#10) TORASEMID (TORASEMIDE) ; 01-APR-2009 / Unknown

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included obesity with BMI of 35.6, hyperuricemia, abuse of diuretics, hyperlipidemia, ischemic heart disease, transient ischemic attack on 23-Nov-2013, hypertension, and chronic gastrointestinal disease on 01-Mar-2008 described as peptic ulcers, GI-bleeding, diverticulitis, and adenomas. The patient was not at anytime exposed to any other erythropoietin-stimulating agent (ESA). Race/ethnicity: Caucasian 20-Jan-2014: English translation of the German discharge letter was received. Additional information was obtained regarding medical history. Additional medical history included NSTEMI 09/09, PTCA and tract stent implant of the RCA 09/09, PTCA BMS of the prox. RCA 05/08, PTCA 2x DES of the prox. LAD 04/08, AV block 1, chronic kidney failure according to KDOQI stage IV, benzodiazepine and alcohol dependency, peptic ulcer 03/08, TIA 12/11, and cardiovascular risk factors which included positive family history, and adiposity. 06-Aug-2014: Additional information was received from the same reporter regarding medical history and death details. Medical history also included interstitial nephritis which led to renal failure diagnosed in 22-Mar-1994. The patient was not on dialysis. Risk factor also included coronary heart disease. The risk factor NSTEMI was also reported as myocardial infarction. On 11-Jul-2014, the patient experienced sudden cardiac death at home. It was not reported if an autopsy was performed. The patient did not complete the study because her death.
Unknown to Ongoing	Relevant Med History	Gastrointestinal tract adenoma (Gastrointestinal tract adenoma); 01-Mar-2008; chronic gastrointestinal disease
Unknown to Ongoing	Relevant Med History	Agitated (Agitation);
Unknown to Ongoing	Relevant Med History	Alcohol addiction (Alcoholism);
Unknown to Ongoing	Relevant Med History	Benzodiazepine dependent (Drug dependence);
Unknown to Ongoing	Relevant Med History	Kidney failure chronic (Chronic kidney disease); according to KDOQI stage IV; diagnosed in 22-Mar-1994
Unknown to Ongoing	Relevant Med History 01-Mar-2008	Diverticulitis (Diverticulitis);
Unknown to Ongoing	Relevant Med History 01-Mar-2008	Gastrointestinal bleeding (Gastrointestinal haemorrhage);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Nephritis interstitial (Tubulointerstitial nephritis);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Nervous (Nervousness);
Unknown to Ongoing	Relevant Med History 01-Mar-2008; 03/08	Peptic ulcer (Peptic ulcer);
Unknown to Ongoing	Relevant Med History 23-Nov-2013; 12/11	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	AV block first degree (Atrioventricular block first degree);
Unknown	Relevant Med History 09/09	Non STEMI (Acute myocardial infarction);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History 09/09	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
Unknown	Relevant Med History 04/08	Drug-eluting coronary stent placement (Coronary arterial stent insertion);
Unknown	Relevant Med History 05/08	Bare metal coronary stent placement (Coronary arterial stent insertion);
Unknown	Relevant Med History 09/09	Coronary arterial stent insertion (Coronary arterial stent insertion);
Unknown	Relevant Med History	Diuretic abuse (Drug abuse);
Unknown	Relevant Med History	Family history of cardiovascular disorder (Familial risk factor);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Hyperuricemia (Hyperuricaemia);
Unknown	Relevant Med History Risk Factor: BMI: 35.6	Obesity (Obesity);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	22	DEC	1919	93 Years	Female	60.00 kg	01	MAR	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Peripheral arterial occlusive disease [Peripheral arterial occlusive disease]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of peripheral arterial
occlusive disease. This serious case from a physician (reference: Ge-097-0013) describes a 93-year-old female patient (weight: 60 kg and height: 165 cm) who received Retacrit (epoetin zeta, subcutaneous, once a week; dose,

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) Freq: 1 Week, Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 09-MAY-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2184107

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-FEB-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

formulation, and batch number not reported) for renal anaemia from 09-May-2011. It was reported that the patient was not previously exposed to other erythropoetin stimulating agent. Concomitant medications were not reported. On 09-May-2011, the patient began treatment with epoetin zeta. On 19-Feb-2013, it was reported that the patient received the last dose of epoetin zeta prior to the adverse event. On 01-Mar-2013, the patient developed peripheral arterial occlusive disease (PAOD) IV also reported as PAVK IV. On the same day, the patient was admitted to the hospital. Treatment for the adverse event and action taken with the suspect drug were not reported. On 19-Apr-2013, the patient was discharged from the hospital. Outcome of the adverse event was reported as persistent /significant disability. The reporter's causality assessment for the event of peripheral arterial occlusive disease in relation to epoetin zeta was not related. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number, and date of expiry.

Case Comment: Overall case causality: Not assessable Cannot provide event causation without objective clinical event details, medical history and concomitant medications, if any. - R. Jacot (19 Feb 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. It was reported that the patient was not previously exposed to other erythropoetin stimulating agent. Race/Ethnicity: Caucasian.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	22	JAN	1934	80 Years	Female	60.00 kg	10	OCT	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Sweden, administered subcutaneously for the treatment of renal anaemia. This report describes a case of myocardial
infarction. This case from a physician (ref: Sw-011-0007) describes an 80-year-old female patient (weight: 60 kg; height: 166 cm) who received Retacrit (epoetin zeta; subcutaneous, every second week; batch number unknown; dose not

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) every second weekNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 10-JAN-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ADENOSIN LIFE MEDICAL (ADENOSINE) Solution for injection ; Unknown
#2) ALVEDON (PARACETAMOL) Tablet ; Unknown
#3) AMLODIPIN ACCORD (AMLODIPINE BESILATE) ; Unknown
#4) ARIXTRA (FONDAPARINUX SODIUM) Solution for injection in pre-
#5) BRILIQUE (TICAGRELOR) Tablet ; Unknown
#6) FURIX (FUROSEMIDE) Solution for injection ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2195433

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-MAR-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

reported) for renal anaemia since 10-Jan-2013. Medical history included peritoneal dialysis, hyperlipidemia, diabetes mellitus, hypertension, and polycystic kidney disease which started at birth. It was reported that the patient was not at any time exposed to any other erythropoetin-stimulating agent (ESA). Concomitant medications included Novorapid Flexpen 100 U/mL, Novorapid 100 U/mL, Lantus Solostar 100 units/mL, Kaleorid 750 mg, Trombyl 75 mg, metoprolol Sandoz 100 mg, simvastatin Sandoz 20 mg, Renvela 800 mg, Brilique 90 mg, Arixtra 1.5 mg/0.3 ml, metoprolol Ratiopharm 50 mg, citalopram Orion 20 mg, glucose B.Braun 50 mg/mL, amlodipine Accord 10 mg, heparin Leo 5000 IU/mL, nitroglycerin BMM Pharma 0.1 mg/mL, Adenosin Life Medical 40 mcg/mL, Iomeron 300 mg/mL, Glytrin 0.4 mg/dose, Tradolan 50 mg, Alvedon 500 mg, Movicol, Furix 10 mg/mL, Seloken 50 mg, Xylocain 10 mg/mL, Stesolid Novum 5 mg/mL, Kinin Recip 100 mg, and illegible (doses and routes of administration not reported), all for unknown indications. On 10-Jan-2013, the patient received the first dose of epoetin zeta. The patient received the last dose prior to the event on 03-Oct-2013.
On 10-Oct-2013, the patient experienced myocardial infarction manifested by chest pain. On the same day, the patient was hospitalized. The adverse event was described as a small cardiac infarction (NSTEMI). Troponin T on the same day at 16:24 was 170 ng/L, 732 ng/L at 23:02, and 3000 ng/L on 11-Oct-2013 at 07:56 (normal value: less than 15). On an unknown day, coronary angiography showed only small peripheral occlusion of LCX. Action taken with epoetin zeta was not reported. Treatment for the adverse event included Arixta and Brilique (doses and routes of administration not reported) prescribed for a month. On 14-Oct-2013, the patient completely recovered from the event of myocardial infarction and was discharged from the hospital on the same day. The reporter's causality assessment of the event of myocardial infarction in relation to epoetin zeta was unlikely. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: dosage administered. 05-Mar-2014: English translation of the Swedish discharge letter from the investigator was received. Follow up report was created to reflect additional information regarding the patient's medical history, adverse event, diagnostic tests, and concomitant medications. Diabetes mellitus was further described as diabetes mellitus type 2 with unspecified complications. Additional medical history included chronic kidney failure (secondary), non-specific, diabetes retinopathy, and essential hypertonia. Dosage forms of concomitant medications were injection on pre-filled syringe for Novorapid, Lantus, and Arixtra; extended-release tablets for Kaleorid (potassium chloride), metoprolol Sandoz, and metoprolol Ratiopharm; film-coated tablets for simvastatin Sandoz, Renvela, Brilique, citalopram, Tradolan, Alvedon, and Kinin Recip; tablets for Furix, Seloken, amlodipin Accord, Trombyl (aspirin), and the illegible drug product; infusion on liquid, solution for glucose B.Braun, heparin Leo, adenosine Life Medical, Iomeron, and xylocaine; concentrate infusion liquid, solution for nitroglycerin; sublingual spray for glytrin; powder for oral solution in dose sachet for Movicol; and injection on liquid, emulsion for Stesolid Novum. The adverse event of myocardial infarction was further described as non-ST segment elevation myocardial infarction and acute subendocardial infarction. It was reported that the patient arrived at the hospital with pressure pain in the chest related to an uphill walk, feeling sick, and in a cold sweat. At emergency, the patient was sensitive to pain, in chest, and with high blood pressure at 210/100 (unit of measurement and normal value not reported). The patient became pain-free with Nitro (dose and route of administration not reported). The patient was also given amlodipine and Furix (doses and routes of administration not reported). Trop with dynamics, for which reason was given Arixta in addition to ASA (doses and routes of administration not reported). The next day, Brilique was also added before coronary angiography which showed only peripheral occlussion in LCX, stenotic segment downstream from large marginal branch, LAD RCA unremarkable, distal occlussion; continues with conservative treatment over the weekend. It was reported that the patient also sufferred from minor shortness of breath. Coronary echocardiography on 14-Oct-2013 in 2 D/M-mode showed normal width aortic root (30 mm) and aorta ascendens (33 mm). Tricuspid aorta valve that opens normally. Left auricle was enlarged (59 ml/m2). Mitral valve had a normal pattern of movement. Concentric sclerosis. Left atrium had a normal internal diameter (43 mm end diastolic). Septum 15 mm, posterior wall 14 mm. Akenesia basally and mid inferolaterally, basally and mid-antero-laterally, and basally inferiorally; other wall segments were hyperkinetic. EF was estimated according to Simpson with a contrast of 49%. Right auricle was of normal size (12 cm2). Right atrium was of normal size (RVOT-diameter 23 mm), the right chamber difficult to image in apical 4-chamber view). Normal mobility in the free wall of the right atrium (AVR 24 mm). Inferior V cava was of normal width (14 mm), normal breathing variation cannot be determined. Intracoronary-ultrasound and Doppler showed aorta at max. 1.4 m/s. LVOT max. 0.9 m/s. Mitralis E/A 0.6. E/E' average. E/E' average 14; low tissue velocities. Insignificant mitral insufficiency. Minor tricuspid insufficiency with at max. 2.5 m/s, which probably gave a normal systolic PA-pressure regardless of whether the vena cava inferior was subjected to variable respiration or not. In summary, assessment was moderate concentric VKH (left chamber hypertrophy, akenesia basally and mid-inferiolaterally, basally and mid-antero-laterally, as well as basally inferiorally. EF was estimated according to Simpson with a contrast of 49%. There were symptoms of diastolic dysfunction with E/E'14; normal HKF (right chamber function); probably normal systolic PA pressure; no valve abnormalities. EKG showed sinus rhythm at 70/min. Patol-R wave progression V3 and T-wave progression V3-V4. Laboratories included trop 170-732-3000, creatinine 439-559, and potassium 3.4-4.1 (units of measurement and normal values not reported). Healthy and uncomplicated progress. X-ray of lungs unremarkable. It was reported that the adverse event cleared up on its own. In consideration of the peritoneal dialysis, the patient was prescribed to take Brilique for only 1 month up to and including 131114, and after that, ASA.

Case Comment: Overall case causality: Probably not Patient has several cardiovascular risk factors for myocardial infarction. - R. Jacot (18 Feb 2014) Follow-up (11 Mar 2014): No change in previous company assessment. - R. Jacot

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Angiogram	Small peripheral occlusion of LCX, Unknown	
2		Angiogram	LAD RCA unremarkable, Unknown	
3		Angiogram	stenotic segment downstream, Unknown	
4		Angiogram	distal occlusion, Unknown	
5		Angiogram	from large marginal branch, Unknown	
6	14-OCT-2013	Angiogram		
7		Blood pressure measurement	210/100, Unknown	
8	14-OCT-2013	Echocardiogram	moderate concentric left chamber hypertrophy, Unk	
9	14-OCT-2013	Echocardiogram	akenesia basally and mid-inferiolaterally, Unknown	
10	14-OCT-2013	Echocardiogram	basally and mid-antero-laterally, Unknown	
11	14-OCT-2013	Echocardiogram	as well as basally inferiorally, Unknown	
12	14-OCT-2013	Ejection fraction	49 %	
13		Electrocardiogram	T-wave progression V3-V4, Unknown	
14		Electrocardiogram	Patol-R wave progression V3, Unknown	
15		Electrocardiogram	Normal sinus rhythm 70/min; 80/min, Unknown	
16	10-OCT-2013	Troponin T	170, NG/L	
17	10-OCT-2013	Troponin T	732, NG/L	
18	11-OCT-2013	Troponin T	3000, NG/L	
19	14-OCT-2013	Ultrasound Doppler	probably normal systolic PA pressure, Unknown	
20	14-OCT-2013	Ultrasound Doppler	diastolic dysfunction with E/E'14, Unknown	
21	14-OCT-2013	Ultrasound Doppler	normal HKF (right chamber function), Unknown	
22	14-OCT-2013	Ultrasound Doppler	no valve abnormalities, Unknown	

13. Relevant Tests

Coronary echocardiography(14-OCT-2013) : moderate concentric left chamber hypertrophy, Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) ARIXTRA (FONDAPARINUX SODIUM) Solution for injection in pre-filled syringe ; Unknown

#7) FURIX (FUROSEMIDE) Tablet ; Unknown

#8) GLUCOSE B. BRAUN (GLUCOSE) Solution for infusion ; Unknown

#9) GLYTRIN (GLYCERYL TRINITRATE) ; Unknown

#10) HEPARIN LEO (HEPARIN SODIUM) Solution for injection ; Unknown

#11) IOMERON (IOMEPROL) Solution for injection ; Unknown

#12) KALEORID (POTASSIUM CHLORIDE) Tablet ; Unknown

#13) KININ RECIP (QUININE HYDROCHLORIDE) Tablet ; Unknown

#14) LANTUS (INSULIN GLARGINE) ; Unknown

#15) METOPROLOL RATIOPHARM /00376903/ (METOPROLOL SUCCINATE) Tablet ; Unknown

#16) METOPROLOL SANDOZ /00376902/ (METOPROLOL TARTRATE) Tablet ; Unknown

#17) MOVICOL /01749801/ (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE) Oral solution ; Unknown

#18) NOVORAPID (INSULIN ASPART) ; Unknown

#19) RENVELA (SEVELAMER CARBONATE) Tablet ; Unknown

#20) SELOKEN /00376902/ (METOPROLOL TARTRATE) Tablet ; Unknown

#21) SIMVASTATIN SANDOZ (SIMVASTATIN) Tablet ; Unknown

#22) STESOLID NOVUM (DIAZEPAM) Emulsion for infusion ; Unknown

#23) TRADOLAN (TRAMADOL HYDROCHLORIDE) Tablet ; Unknown

#24) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; Unknown

#25) XYLOCAIN /00033402/ (LIDOCAINE HYDROCHLORIDE) Solution for injection ; Unknown

#26) CITALOPRAM (CITALOPRAM) Tablet ; Unknown

#27) NITROGLYCERIN (GLYCERYL TRINITRATE) Concentrate for solution for infusion ; Unknown

#28) OTHER THERAPEUTIC PRODUCTS Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included peritoneal dialysis, hyperlipidemia, diabetes mellitus, hypertension, and polycystic kidney disease which started at birth. It was reported that the patient was not at any time exposed to any other erythropoetin-stimulating agent (ESA). Race/Ethnicity: Caucasian. 05-Mar-2014:Additional information was received from the same reporter regarding medical history. Diabetes mellitus was further described as diabetes mellitus type 2 with unspecified complications. Additional medical history included chronic kidney failure

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	(secondary), non-specific, diabetes retinopathy, and essential hypertonia.	
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Diabetic retinopathy (Diabetic retinopathy);
Unknown to Ongoing	Relevant Med History	Hypertonia (Hypertonia);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Polycystic kidney (Congenital cystic kidney disease);
Unknown	Relevant Med History	Peritoneal dialysis (Peritoneal dialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	22	JUL	1946	67 Years	Female	60.00 kg	08	OCT	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Deep vein thrombosis [Deep vein thrombosis]
Pulmonary embolism [Pulmonary embolism]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia. This report from Germany describes a case of
deep vein thrombosis and possible pulmonary embolism.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2J306K2}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) Freq: 3 week, Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-AUG-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FENISTIL (DIMETINDENE MALEATE) Gel ; Unknown
#2) CETIRIZINE (CETIRIZINE) Tablet ; Unknown
#3) CIPROFLOXACIN (CIPROFLOXACIN) ; Unknown
#4) DOXYCYCLINE (DOXYCYCLINE) ; 15-OCT-2013 / Unknown
#5) IRON (IRON) ; Unknown
#6) LIDOCAINE (LIDOCAINE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Knee osteoarthritis (Osteoarthritis)
Unknown to Ongoing	Relevant Med History	Kidney atrophic (Renal atrophy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2207374

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This serious case from an investigator (ref: Ge-093-0057) describes a 67-year-old female patient (weight: 62 kg, height: 164 cm) who received Retacrit (epoetin zeta, three times a week, subcutaneous, batch number 2J306K2; dose not reported) for renal anaemia on 12-Aug-2013. Medical history included hypothyreosis, hypokalemia, multiple myeloma on an unknown day in Apr 2003 and colitis on an unknown day in Aug 2013. It was reported that the patient was on hemodialysis. It was also reported that the patient was not exposed to any other erythropoietin-stimulating agent. Concomitant medications were not reported. On 12-Aug-2013, the patient started treatment with epoetin zeta. Last dose of epoetin zeta prior to the event was on 07-Oct-2013. On 08-Oct-2013, the patient was admitted to the hospital because of deep vein thrombosis and possible pulmonary embolism. On 08-Oct-2013, thrombophil screening revealed Quick of 96% (70-130), INR of 1.02 (unit and normal value not reported), PTT of 27.5 sec (25.1-36.5), protein C of 87% (70-140), protein S of 82% (53-109), factor VIII of 161% (70-150). Also on the same day of 08-Oct-2013, plasma exchange trial was negative, factor-V-Leiden-Mutation (G1691A) and factor-II-Mutation (G20210A) showed wildtype. On 10-Oct-2013 at 08:20, Quick was 87%, INR was 1.09 and PTT was 28.6 sec. On 11-Oct-2013 at 16:38, Quick was 94.8%, INR was 1.03 and PTT was 100.7 sec. On 14-Oct-2013 at 07:36, Quick was 116%, INR was 0.92 and PTT was 29.8 sec. Treatment for the events and action taken with the suspect drug was not reported. On 15-Oct-2013 at 07:54, Quick was 90%, INR was 1.07, PTT was 29.1 sec and fibrinogen was 492 mg/dl (276-471). Outcome of the events of deep vein thrombosis and possible pulmonary embolism was unknown at the time of the report. However, it was also reported the event stop date was on 15-Oct-2013. The reporter's causality assessment for the events of deep vein thrombosis and possible pulmonary embolism in relation to epoetin zeta was possible. Risk factors for thromboembolic events included homocysteinemia and bone marrow biopsy on 15-Oct-2013. The following information has been requested from the reporter for identification and traceability of the biosimilar product Epoetin zeta: dosage administered. 19-Mar-2014: English translation of the German text was received. Follow-up report was created to reflect new information regarding patient details, medical history, concomitant medications, and laboratory data. Patient's birth date was updated. Patient's height and weight were updated to 169 cm and 60 kg respectively. It was reported that the patient's multiple myeloma was from IgG-lambda type ED. Colitis was also reported as suspected chronic inflammatory bowel disease over the entire colon but was stressed on the right colon. Medical history also included cholecystectomy in 1997, abdominal surgery (hysterectomy) for cervical cancer in 1998, nephritis on both sides in 1999, MGUS ED on an unknown day in Feb-2003, mild hypochromic anaemia (s/p transfusion of 4 RCCs and suspected transfusion reaction on an unknown day in Aug-2013), level II reflux esophagitis with type C gastritis, arthrosis of the knee on both sides, and Novalgin/Tramal intolerance. The patient also had chronic kidney failure also reported as terminal renal insufficiency which required dialysis, atrophic kidney with right greater than the left, multiple renal cysts, recurrent shunt occlusion, currently 2 Demers catheters. Concomitant medications included iron for an unknown indication, mesalazine and prednisolone for chronic colitis with an ischaemic origin, ciprofloxacin for urinary tract infection, cetirizine tablets and Fenistil gel for itching, and L-thyroxine for hypothyroidism (doses and routes of administration not reported); lidocaine (10 ml, subcutaneous) and fractionated propofol (120 mg, intravenous) as premedications; and doxycycline (100 mg, 1-0-1, oral) as antibiotic therapy. It was stated that the patient was admitted on 08-Oct-2013 following referral for inpatient monitoring of the colitis described in Aug-2013. The patient indicated that she had not taken prednisolone (dose and route of administration not reported) recently - as recommended by the physician. It was reported that the patient's stools were still to some extent quite soft and dark from intake of iron. The patient also complained of limited mobility (no strength in her legs) since May-2013 and increasingly painful livid swelling of the right leg over the past few days that started in the lower leg but is now mostly localised in the upper leg. In addition, patient had lost around 11 kg over the last 6 months. The patient clinically presented as a slender woman with reduced overall health, having a soft abdomen with no significant pain on palpation, sparse borborygmus and the livid swelling of the right leg was painful on palpation and accentuated in the right upper leg. It was reported that the puncture site for the Demers catheter was not irritated. On 08-Oct-2013, an abdominal sonograph revealed a thickening of the intestinal wall in the region of the right hemicolon. On the same day, duplex sonograph of peripheral veins revealed distinct deep leg vein thrombosis with extension into the pelvis also reported as complete upper leg/pelvic vein thrombosis on the right. It was reported that a thoracic CT was not done because of a discrete hyperventilation tendency in the patient (BGA) due to the terminal kidney failure (but with residual excretion). On 08-Oct-2013, laboratory result included elevated homocysteine of 33.3 mcmol/l (normal value: less than 13.9 mcmol/l) as well as a high factor VIII level. As a hyperhomocysteinemia occured with a vitamin B deficiency, appropriate tests were carried out which revealed folic acid and vitamin B12 deficiencies. It was reported that a substitution for which was recommended. After the correction of folic acid and vitamin B12, it was reported that the homocysteine level should be determined again. On 09-Oct-2013, an echocardiograph was carried out which revealed inferior vena cava not easily delimited, appeared somewhat filled, but no thrombus can be definitively detected, no indication of acute right ventricular load, but slight accentuation of the right heart cavities and septum dyskinesia that could be consistent with peripheral pulmonary embolism. On the same day, the pleural sonograph of both sides showed peripheral embolisms basally on both sides, with small infiltrate/effusion on the right, post-stenotic. It was reported that the echocardiograph and pleural sonograph indirectly indicated peripheral pulmonary embolisms. It was also reported that the elevated ProBNP corroborated these findings. Also on 09-Oct-2013, urine culture detected the formation of ESBL (E.coli, Proteus mirabilis and Klebsiella spp.) On 10-Oct-2013, neurology consultation was done that showed weakness in both legs caused by immobility. There was no evidence of neurological process like events. The patient was recommended to be relocated to rehabilitation. Laboratory chemistry work revealed an M-spike in the protein electrophoresis on 10-Oct-2013 and 12-Oct-2013. This led to the suspicion of multiple myeloma, which could also be the cause for the thrombophilia, anaemia (now only mild), kidney failure and also an indirect cause for the colitis. On 10-Oct-2013, serological analysis indicated pathological values for the following: albumin was 47.1% (normal range: 53-65.1%), beta-2-microglobulin was 12 mg/l (normal

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

range: 0.61-2.37 mg/l), albumin-globulin quotient was 0.89 (normal range: 1.15-1.86; unit not reported), IgG was 1520 mg/dl (normal range: 390-1050 mg/dl), IgA was 92 mg/dl (normal range: 70-500 mg/dl), total lambda light chains was 1480 mg/dl (normal range: 313-723 mg/dl), free lambda light chains was 8.65 mg/dl (normal range: 0.571-2.63 mg/dl), and total kappa/lambda quotient was 0.28 (normal range: 1.53-3.29; unit not reported). Also on 10-Oct-2013, a colonoscopy was done which presented a chronic colitis that was consistent with an ischaemic origin. In addition to mesalazine, treatment for this with prednisolone was resumed. As a secondary finding, the patient was treated for urinary tract infection with ciprofloxacin. On 11-Oct-2013, a bone marrow puncture was performed for suspected multiple myeloma which showed that the criteria for a monoclonal gammopathy of undetermined significance (MGUS) were met in the bone marrow and there was also significantly toxic bone marrow damage; premedication included lidocaine and propofol and there were no complications. It was also reported that the plasma cell percentage in bone marrow was 10%. It was stated that the MGUS which was identified in Feb-2003 had apparently transitioned to a multiple myeloma in the interim. On the same day of 11-Oct-2013, low-dose CT scans showed no osseous destruction (secondary finding: a small meningioma). On 12-Oct-2013, serological analysis indicated pathological values for the following: albumin was 48.0%, beta-2-microglobulin was 6.91 mg/l, albumin-globulin quotient was 0.92, IgG was 1700 mg/dl, IgA was 103 mg/dl, total lambda light chains was 1680 mg/dl, free lambda light chains was 5.96 mg/dl, and total kappa/lambda quotient was 0.27 (normal range: 1.53-3.29; unit not reported). All of these findings amount to the multiple myeloma (until now, ISS Stage III and IB after Salmon and Durie). It was reported that at least 2 CRABB criteria were met and there was indication for treatment. It was reported that the patient's leg was wrapped and kept cool for the thrombosis. Pain therapy (unspecified) was adjusted, compression stockings were ordered and anticoagulation with heparin preservation using Marcumar was initiated. It was stated that Rivaroxaban, Dabigatran and Apixaban were contraindicated due to renal insufficiency. On an unknown date, the patient complained of itching; cetirizine and Fenistil were added to the medication. Also on an unknown date, the patient began treatment with L-thyroxin. Prior to discharge, there was a change to the correct antibiotic therapy with doxycycline. No ESBL formation was detected in the nose/throat swab and anal swab on 14-Oct-2013. On 15-Oct-2013, laboratory result included elevated TPO antibodies (Anti-TPO) of 429 U/ml (normal value: less than 60 U/ml) which suggested Hashimoto's thyroiditis. On the same day, the patient was discharged in a stable clinical condition to outpatient care.

Amendment: This follow-up report is being submitted to amend previously reported information: hospitalization ticked for both events (Deep vein thrombosis, Pulmonary embolism) as seriousness criteria; hospitalization details added.

Case Comment: Overall case causality: Possible Temporally related and labeled events, but consider also contributory effects of relevant medical history and other risk factors for thromboembolism. - R. Jacot (04 Mar 2014) Follow-up (03 Apr 2014): No change in assessment. - R. Jacot

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-OCT-2013	Activated partial thromboplastin time	27.5 seconds	36.5 25.1
2	10-OCT-2013	Activated partial thromboplastin time	28.6 seconds	36.5 25.1
3	11-OCT-2013	Activated partial thromboplastin time	100.7 seconds	36.5 25.1
4	14-OCT-2013	Activated partial thromboplastin time	29.8 seconds	36.5 25.1
5	15-OCT-2013	Activated partial thromboplastin time	29.1 seconds	36.5 25.1
6	10-OCT-2013	Albumin globulin ratio	0.89, Unknown	1.86 1.15
7	12-OCT-2013	Albumin globulin ratio	0.92, Unknown	1.86 1.15
8	14-OCT-2013	Anti-thyroid antibody	429 IU/ml	
9	11-OCT-2013	Aspiration bone marrow	Criteria for a MGUS were met, Unk	
10	11-OCT-2013	Aspiration bone marrow	Significantly toxic bone marrow damage, Unk	
11	11-OCT-2013	Aspiration bone marrow	Plasma cell percentage in	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			bone marrow was 10%, Unk	
12	10-OCT-2013	Beta 2 microglobulin	12 mg/l	2.37 0.61
13	12-OCT-2013	Beta 2 microglobulin	6.91 mg/l	2.37 0.61
14	10-OCT-2013	Blood albumin	47.1 %	65.1 53
15	12-OCT-2013	Blood albumin	48 %	65.1 53
16	15-OCT-2013	Blood fibrinogen	492 mg/dl	471 276
17	08-OCT-2013	Blood homocysteine	33.3, MCMOL/L	
18	10-OCT-2013	Blood immunoglobulin A	92 mg/dl	500 70
19	12-OCT-2013	Blood immunoglobulin A	103 mg/dl	500 70
20	10-OCT-2013	Blood immunoglobulin G	1520 mg/dl	1050 390
21	12-OCT-2013	Blood immunoglobulin G	1700 mg/dl	1050 390
22	08-OCT-2013	Coagulation factor VIII level	161 %	150 70
23	10-OCT-2013	Colonoscopy	Chronic colitis with an ischaemic origin, Unk	
24	11-OCT-2013	Computerised tomogram	Small meningioma, Unk	
25	11-OCT-2013	Computerised tomogram	No osseous destruction, Unk	
26	14-OCT-2013	Culture	No ESBL formation, Unk	
27	14-OCT-2013	Culture	No ESBL formation, Unknown	
28	09-OCT-2013	Culture urine	Formation of ESBL, Unk	
29	09-OCT-2013	Culture urine	E.coli, Proteus mirabilis, and Klebsiella spp, Unk	
30	09-OCT-2013	Echocardiogram	Peripheral pulmonary embolisms, Unk	
31	10-OCT-2013	Electrophoresis protein	M-spike, Unk	
32	12-OCT-2013	Electrophoresis protein	M-spike, Unk	
33	08-OCT-2013	International normalised ratio	1.02, Unknown	
34	10-OCT-2013	International normalised ratio	1.09, Unknown	
35	11-OCT-2013	International normalised ratio	1.07, Unknown	
36	14-OCT-2013	International normalised ratio	0.92, Unknown	
37	15-OCT-2013	International normalised ratio	1.07, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
38	08-OCT-2013	Laboratory test	Negative, Unknown	
39	08-OCT-2013	Laboratory test	Wildtype, Unknown	
40	08-OCT-2013	Laboratory test	Wildtype, Unknown	
41	10-OCT-2013	Light chain analysis	1480 mg/dl	723 313
42	10-OCT-2013	Light chain analysis	0.28, Unknown	3.29 1.53
43	10-OCT-2013	Light chain analysis	8.65 mg/dl	2.63 0.571
44	12-OCT-2013	Light chain analysis	5.96 mg/dl	2.63 0.571
45	12-OCT-2013	Light chain analysis	1680 mg/dl	723 313
46	12-OCT-2013	Light chain analysis	0.27, Unknown	3.29 1.53
47		N-terminal prohormone brain natriuretic peptide	Elevated,Unknown	
48	10-OCT-2013	Neurological examination	Weakness in both legs caused by immobility, Unk	
49	08-OCT-2013	Protein C	87 %	140 70
50	08-OCT-2013	Protein S	82 %	109 53
51	08-OCT-2013	Prothrombin time	96 %	130 70
52	10-OCT-2013	Prothrombin time	87 %	130 70
53	11-OCT-2013	Prothrombin time	94.8 %	130 70
54	14-OCT-2013	Prothrombin time	116 %	130 70
55	15-OCT-2013	Prothrombin time	90 %	130 70
56	08-OCT-2013	Ultrasound Doppler	Complete deep leg vein thrombosis on the right	
		revealed distinct deep leg vein thrombosis with extension into the pelvis also reported as complete upper leg/pelvic vein thrombosis on the right		
57	08-OCT-2013	Ultrasound Doppler	Peripheral pulmonary embolisms	
58	08-OCT-2013	Ultrasound abdomen	Thickening of the intestinal wall, Unk	
59	08-OCT-2013	Ultrasound abdomen	In the region of the right hemicolon, Unk	
60	09-OCT-2013	Ultrasound chest	Peripheral pulmonary embolisms, Unk	

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) L-THYROXINE /00068001/ (LEVOTHYROXINE) ; Unknown

#8) MESALAZINE (MESALAZINE) ; Unknown

#9) PREDNISOLONE (PREDNISOLONE) ; Unknown

#10) PROPOFOL (PROPOFOL) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Cervical cancer (Cervix carcinoma);
Unknown to Ongoing	Relevant Med History	Kidney failure chronic (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Folic acid deficiency (Folate deficiency);
Unknown to Ongoing	Relevant Med History	Hypokalemia (Hypokalaemia);
Unknown to Ongoing	Relevant Med History	Hypothyreosis (Hypothyroidism);
Unknown to Ongoing	Relevant Med History	Reflux esophagitis (Gastrooesophageal reflux disease);
Unknown to Ongoing	Relevant Med History Feb-2003	MGUS (Hypergammaglobulinaemia benign monoclonal);
Unknown to Ongoing	Relevant Med History	Hypochromic anaemia (Hypochromic anaemia);
Unknown to Ongoing	Relevant Med History In Apr 2003; IgG-lambda type ED	Multiple myeloma (Plasma cell myeloma);
Unknown to Ongoing	Relevant Med History	Renal cyst (Renal cyst);
Unknown to Ongoing	Relevant Med History	Shunt occlusion (Shunt occlusion);
Unknown to Ongoing	Relevant Med History	Hashimoto's thyroiditis (Autoimmune thyroiditis);
Unknown to Ongoing	Relevant Med History	Gastritis (Gastritis);
Unknown to Ongoing	Relevant Med History	Urinary tract infection (Urinary tract infection);
Unknown to Ongoing	Relevant Med History	Vitamin B12 deficiency (Vitamin B12 deficiency);
Unknown	Relevant Med History	Vascular catheterisation (Vascular catheterisation);
Unknown	Relevant Med History 1998	Abdominal hysterectomy (Hysterectomy);
Unknown	Relevant Med History 1997	Cholecystectomy (Cholecystectomy);
Unknown	Relevant Med History In Aug 2013	Colitis (Colitis);
Unknown	Relevant Med History	Nephritis (Nephritis);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	1999	
Unknown	Relevant Med History	Drug intolerance (Drug intolerance);
Unknown	Relevant Med History	Transfusion reaction (Transfusion reaction);
Unknown	Relevant Med History Risk Factor-In 11-Oct-2013	Bone marrow biopsy (Biopsy bone marrow);
Unknown	Relevant Med History Risk Factor	Homocystinemia (Homocystinaemia);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
Unknown	Past Drug Event	NOVALGIN (NOVALGIN /00169801/); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Drug intolerance (Drug intolerance)
Unknown	Past Drug Event	TRAMAL (TRAMAL); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Drug intolerance (Drug intolerance)
Unknown	Past Drug Event Action taken:Not applicable	PREDNISOLONE (PREDNISOLONE);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	FEB	1936	78 Years	Female	75.50 kg	03	APR	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Non elevated myocardial infarction [Acute myocardial infarction]
Thromboembolic event [Embolism]
Angiodysplasia [Angiodysplasia]

Case Description: Angiodysplasia, non elevated myocardial infarction and thromboembolic event. Epoetin Zeta. Hospira-sponsored study report from Germany, received from an investigator (Ge-165-0002), which refers to a patient.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3E359F3; Exp.Dt. 01-AUG-2015}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 26 IU/kg/w (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 22-OCT-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) JANUVIA (SITAGLIPTIN PHOSPHATE) ; Unknown
#2) OSVAREN (CALCIUM ACETATE, MAGNESIUM CARBONATE) ; Unknown
#3) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown
#4) TARGIN (NALOXONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE) ; Unknown
#5) AMIODARONE (AMIODARONE) ; Unknown
#6) ASA (ACETYLSALICYLIC ACID) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History 06-Aug-2005	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2294363

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-NOV-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient was not pregnant at the time of treatment and had no known drug hypersensitivities or history of drug dependence. Medical history included myocardial failure NYHA II, status post triple ACVB surgery (LIMA to RIVA, 2 ACVB to RCX and RPD May-1999), atrial fibrillation since 06-Aug-2005, DDDR pacemaker for post ablation of an isthmus-dependent atrial flutter in Mar-2010, severe stenosis of the aortic bifurcation with intermittent claudication IIb both sides, hyperlipidemia since 28-Jul-2010, peripheral arterial disease since 28-Jul-2010, diabetic nephropathy which led to the diagnosis of chronic dialysis-dependent kidney failure stage V, hypertensive nephrosclerosis (confirmed by histology Aug-2010), on hemodialysis 3 times per week since 26 Jul 2011, cancer since 30-Dec-2012, status post upper lobe resection in Jan-2013 for bronchial carcinoma (Tx, N0, M0), status post LAD-PTCA with implant of a DES (12-Dec-2013), 3-vessel coronary artery disease with non-invasive exclusion of a CHD progression in 18-Mar-2014, shunt insertion left cubital fossa, nephrotic and nephritic syndrome and secondary renal hyperparathyroidism. The patient had not been treated with other erythropoietin stimulating agents (ESA) and had no previous exposure to other biosimilars. Concomitant medications included Januvia, torasemide, xipamide, Bondiol, Ossvaren, clopidogrel (Plavix), ramipril, bisoprolol, amiodarone, Targin, atorvastatin, Dekristol, Mimpara and ASA. It was also reported that phenprocoumon (Marcumar) was paused. On 22-Oct-2012, the patient started to receive treatment with epoetin zeta (Retacrit, lot number: 3E359F3 and 5O021Q5, 26 IU/kg/week, subcutaneous, 2 dosages per week) for renal anaemia. It was reported that the patient had exertional dyspnoea progressive since December 2013. One week from the time admission, the patient had flu-like infections with no clear focus and was treated with antibiotics (unspecified; dose and route of administration not reported). On the night before the admission, the patient had massive thoracic constriction and general discomfort. According to the patient, she experienced the same symptoms as 15 years ago with myocardial infarction. The patient was admitted on 13-Mar-2014. Admission as an inpatient took place due to the symptoms listed above and for further examination and treatment. Physical examination findings showed that the patient was in reduced overall condition and adipose nutritional status. The patient was conscious, oriented in all respects. RR was reported as 175/80 mmHg, HR was 63/min, and SpO2 at 93% in room air. Coronary was rhythmic. Pulmonary showed vesicular breath sounds on sides, no crepitations, no wheezing, no stridor. Abdomen was soft, no pain on palpation, no muscular guarding. Peristalsis was normal. Skin and mucosa were non-irritated. Course of neurological exam revealed no abnormalities. ECG on admission showed SM-ECG, marked left axis deviation, LBBB, HR 72/min, S to V6, ST(-T)-segment changes caused by block. On 13-Mar-2014 at 12:19, laboratory tests were done that showed CK at 128 U/L (normal values: 1-200), CK-MB at 12 U/L (normal values:1-24), triglyceride at 97mg/dl (normal values: 1-200), cholesterol at 162 mg/dL (normal values: 1-200), Quick test at 41% (normal values: 82-130), INR at 1.76 (normal values: 0.86-1.27), PTT at 31 (normal values: 20-33), and troponin T at 43 pg/ml (normal value: less than 14). On 13-Mar-2014 at 15:36, laboratory tests were done that showed CK at 131 U/L, CK-MB at 11 U/L, and troponin T at 43 pg/ml. On 14-Mar-2014 at 13:02, laboratory tests were done that showed CK at 103, CK-MB at 14, Quick test at 35 %, INR at 2.04, and PTT at 31 sec. Laboratory chemistry and electrocardiography allowed exclusion of an acute coronary infarction. Thoracic x-ray was done on an unknown date that showed pacemaker on right with atrial and ventricular probe. Borderline large heart. Sternotomy after cardiac surgery. Slight hypoventilation in left mid-field, otherwise staple seam in right upper lung field, status post partial lung resection. No definite signs of congestion, no evidence of infiltrate or effusion. Stress echocardiography (dynamic/pharmacologic) was done to further investigate and showed: At rest, global still normal LV function with akinesia of the basal posterior wall and basal IVS (aneurysm). With low-dose Dobutamine stimulation, there was increase in contractility in all wall segments (previously not akinetic). With high-dose Dobutamine stimulation, there was further increase in contractility with no evidence of new regional wall motion abnormalities. In the recovery phase, there was restoration of the initial findings. Assessment was that there was no evidence of ischemia under stress criteria with s/p posterior wall infarction with formation of posterior wall aneurysm. On 17-Mar-2014, laboratory tests were done that showed CK at 85 U/L, CK MB at 17 U/L, Quick at 35 %, INR at 2.06, and PTT at 32 sec. On 18-Mar-2014, the patient was discharged with stable overall condition. On 02-Apr-2014, the patient was admitted to the hospital. On 03-Apr-2014, the patient experienced non elevated myocardial infarction manifested as angina pectoris. Treatment included drug eluting stenting RCA.
No action was taken with the suspect drug in response to the event. The adverse event and hospitalization was ongoing at the time of the report. On 13-Aug-2015, haemoglobin was 8.3 g/ dL (11.2-15.7), haematokrit was 25.7 % (34.1-44.9), MCV was 98.5 fL (79.4-94.8), MCH was 31.8 pg (25.6-32.2), MCHC was 32.3 g/dL (32.0-36.0), leukocytes was 9.2/nL (4.2-9.1), erythrocytes was 2.6/pl (4.6-6.1) and thrombocytes was 284/nL (150-400). On 18-Aug-2015, haemoglobin was 8.8 g/ dL, haematokrit was 26.4%, MCV was 100 fL , MCH was 33.3 pg, MCHC was 33.3 g/dL, leukocytes was 8.1/nL, erythrocytes was 2.6/pl and thrombocytes was 306/nL. On 24-Aug-2015 at 21:45, haematokrit was 27 %. It was reported that a decrease in Hb values led to plan a gastroscopy. On 26-Aug-2015, the patient was admitted to the hospital for further clarification of anaemia with a decrease in hemoglobin by several points since Jul-2015. There was no clinical indication of bleeding stigmata. On an unknown date, the stool guaiac test at the GP was negative. Physical examination findings showed that the patient was in stable condition and good dietary status, awake and oriented to person, place and time. Cor was pure and rhythmic, 4/6 holosystolic (known), pulmo: vesicular respiratory sound on sides, no rattling sounds, breathing frequency was approximately 16 (unit of measurement and normal range not reported). Abdomen was soft, no pressure pain, no muscular defence, peristaltic, regular. The spinal column was without pain on percussion, renal bed free, lower leg free of oedema, no pressure pain in the calf and rough orientating neurological examination was normal. ECG on admission using pacemaker ECG was indifference type, normal heart rate. On an unknown date, leucocytes was at 75 x 10^3/mcL (4.3-10.8), erythrocytes was 2.76 x 10^6/mcl (4.0-5.3), haemoglobin was 9.1 g/dL (12.0-16.0), RDW was 17.3 % (11.5-14.5) and thrombocytes was 266 x 10^3/mcL (140-400). On 27-Aug-2015, gastroscopy was performed and

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

showed an erythematous antral gastritis and two angiodysplasia in in the proximal corpus, large curvature side which was the cause of the source of bleeding and was being treated with APC. Histology showed slight active gastritis of the reactive type, no indication of malignancy. On 28-Aug-2015, colonoscopy was performed and massive residual contamination was noted with a polyp bud in the transversum which was removed using forceps with subsequent oozing bleeding and successful clip application. The mucous membrane was examined without finding the source of bleeding.
The patient was diagnosed with upper gastrointestinal bleeding with angiodysplasia in the body with macrocytic normochromic anaemia with Hb at 7.8 g/dL. On an unknown date, Hb was at 7.5 and the patient was transfused with 1 erythrocyte concentrate due to dyspnea and dizziness which was well tolerated and there was a relevant increase in Hb. On 31-Aug-2015, the patient was discharged status post polypectomy in the colon transversum histological. It was reported that Retacrit administration was still ongoing. Outcome of the event of angiodysplasia was recovered on 01-Sep-2015. It was also reported that the event persisted for 1 day. In the case of reappearance of gastrointestinal bleeding, it was recommended to stop clopidogrel. It was reported that on discharge, the patient was informed that the doctor providing further treatment may be forced to prescribe another preparation to the one given in the clinic due to multitude of medications available with the same purpose without the basic treatment changing as a result of this. On 02-Sep-2015, at 21:19, haematokrit was 28%. On 07-Sep-2015, haemoglobin was 8.6 g/ dL, haematokrit was 26.2%, MCV was 98.9 fL , MCH was 32.5 pg, MCHC was 32.8 g/dL, leukocytes was 9.6/nL, erythrocytes was 2.7/pl , thrombocytes was 307/nL, lymphocytes was 17.1 % (19.0-52.0), monocytes was 13.3% (5.0-13.0), neutrophils was 65.2% (34.0-71.0), eosinophils was 3.6 % (1.0-6.0) and serum iron was 34 mcg/dL (33-193). On 14-Sep-2015, haemoglobin was 11.9 g/ dL, haematokrit was 36.4%, MCV was 96.8 fL , MCH was 31.6 pg, MCHC was 32.7 g/dL, leukocytes was 9.3/nL, erythrocytes was 3.8/pl and thrombocytes was 317/nL. On 05-Oct-2015, haemoglobin was 11.4 g/ dL, haematokrit was 34.7%, MCV was 95.6 fL , MCH was 31.4 pg, MCHC was 32.9 g/dL, leukocytes was 8.8/nL, erythrocytes was 3.6/pl, thrombocytes was 316/nL, lymphocytes was 15.7 % , monocytes was 11.5%, neutrophils was 66%, eosinophils was 6 %, and serum iron was 36 and 32 mcg/dL.
On an unknown date, at the 36-month time point, the patient experienced a thromboembolic event. Current dose of Retacrit prior to the event was 6000 IU/week. Laboratory or diagnostic information, treatment, action taken with epoetin zeta and outcome of the thromboembolic event was not provided. It was reported that the patient had completed the study on 19-Oct-2015. The reporter's opinion of causality between the event of non elevated myocardial infarction and epoetin zeta was unlikely, while not related for the event of vascular abnormality. The reporter's opinion of causality between the thromboembolic event and epoetin zeta was not provided. Risk factors included coronary heart disease also reported as 3-vessel coronary artery disease, vascular anomalies, posterior myocardial infarction 1999 with aneurysm associated with posterolateral akinesia, end stage renal disease, ischemic heart disease since 02-Apr-2014, type 2 diabetes mellitus without vascular complications also reported as Type 2 diabetes mellitus, non-insulin-dependent since 27-Aug-2010, arterial hypertension, hyperlipoproteinaemia, and former nicotine abuse also reported as ex-smoker. 30-Apr-2014: English translation of German discharge letter was received. Follow up report received regarding patient date of birth; dose, frequency, and therapy start date of the suspect drug; further details on medical history, laboratory/diagnostic data, and concomitant medications. This information has been incorporated in the narrative and in the corresponding data fields. 13-Jun-2014: Additional information was received from the investigator regarding action taken with the suspect drug in response to the event. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars and batch number. This information has been incorporated in the narrative and in the corresponding data fields. 01-Sep-2015: Additional information was received from the same reporter. Gastroscopy with coagulation of a vascular abnormality was added as an adverse event. Routes of administration and indications of Januvia and Bondiol were added; doses, routes of administration and indications of torasemide and xipamide were also provided. Ossvaren was added as a concomitant medication. Hb result on 18-Aug-2015 was added. It was reported that a decrease in Hb values led to plan a gastroscopy.
Therapy start date of Retacrit was updated to 22-Oct-2012 (previously 23-Oct-2012). Date of first dialysis was updated (previously Jul-2011); frequency was also added. The patient was not pregnant at the time of treatment and had no known drug hypersensitivities or history of drug dependence. This information has been incorporated in the narrative and in the corresponding data fields. 20-Oct-2015: Additional information was received from the same reporter. Thromboembolic event at the 36-month time point was added. It was reported that the patient had completed the study on 19-Oct-2015. This information has been incorporated in the narrative and in the corresponding data fields. 27-Oct-2015: Additional information was received from the same reporter. It was reported that the patient also received Retacrit lot number: 5O021Q5. Current dose of Retacrit prior to the thromboembolic event at 36th-month point was 6000 IU/week. This information has been incorporated in the narrative and in the corresponding data fields. 03-Nov-2015: Additional information was received from the same reporter. Start date of diabetes mellitus was updated from 28-Aug-2010 to 27-Aug-2010. Adverse event reported term gastroscopy with coagulation of a vascular abnormality was updated to vascular abnormality. It was reported that the patient was admitted to hospital from 26-Aug-2015 to 31 Aug-2015 because of the event of vascular abnormality. Recovery date of vascular abnormality was also provided. Haemoglobin, haematokrit, MCV, MCH, MCHC, leukocytes, erythrocytes, thrombocytes, lymphocytes, monocytes, neutrophils, eosinophils and serum iron results werealso added. This information has been incorporated in the narrative and in the corresponding data fields. Data entry correction was also made to reflect company causality in the data fields for Retacrit with lot number 5O021Q5. 18-Nov-2015: Translation of German text was received. Generic names of Plavix and Marcumar were added. Adverse event reported term vascular abnormality was updated to angiodysplasia and onset date was updated from 31-Aug-2015 to 27-Aug-2015. It was reported that the patient was admitted for further clarification of anaemia with a decrease in hemoglobin by several points since Jul-2015. There was no clinical indication of bleeding stigmata. On an unknown date, the stool guaiac test at the GP was negative. Physical examination findings, ECG on admission leucocyte, erythrocyte, haemoglobin, haematocrit, MCV, MCH, MCHC, RDW and thrombocyte results on an unknown date were added. Gastroscopy with histology on and colonoscopy results on 27-Aug-2015 and 28-Aug-2015, respectively, were also provided. The patient was treated with APC therapy and was transfused with 1 erythrocyte concentrate due to dyspnoea and dizziness

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

which was well tolerated and there was a relevant increase in Hb. The patient was diagnosed with upper gastrointestinal bleeding with angiodysplasia in the body with macrocytic normochromic anaemia with Hb at 7.8 g/dL. On an unknown date, Hb was at 7.5. In the case of reappearance of gastrointestinal bleeding, it was recommended to stop clopidogrel. The patient was status post polypectomy in the colon transversum histological It was reported that on discharge, the patient was informed that the doctor providing further treatment may be forced to prescribe another preparation to the one given in the clinic due to multitude of medications available with the same purpose without the basic treatment changing as a result of this. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Probably not Noting reporter's assessment, the events are more likely due to the patient's underlying cardiac conditions with contributory effects from pre-existing and predisposing risk factors. Follow-up: No change in previous causality assessment. Follow-up: New information noted. The event of gastroscopy with coagulation of vascular abnormality is not related as this is a procedure performed to correct an underlying condition, and not due to the suspect drug. Follow-up: No change in previous assessment. Follow-up: Overall case causality: Possible Hospira causality: Not assessable Newly added adverse event of thromboembolic event cannot be assessed due to limited information as to type and location of event. Follow-up: Updates noted, but no change in previous assessment. Follow-up: No change in assessment. Follow-up: Updates noted. Causality assessment remains the same.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	13-MAR-2014	Activated partial thromboplastin time	31 seconds	33 20
2	14-MAR-2014	Activated partial thromboplastin time	31 seconds	33 20
3	17-MAR-2014	Activated partial thromboplastin time	32 seconds	33 20
4	13-MAR-2014	Blood cholesterol	162 mg/dl	200 1
5	13-MAR-2014	Blood creatine phosphokinase	128 IU/l	200 1
6	13-MAR-2014	Blood creatine phosphokinase	131 IU/l	200 1
7	14-MAR-2014	Blood creatine phosphokinase	103 IU/l	200 1
8	17-MAR-2014	Blood creatine phosphokinase	85 IU/l	200 1
9	13-MAR-2014	Blood creatine phosphokinase MB	11 IU/l	24 1
10	13-MAR-2014	Blood creatine phosphokinase MB	12 IU/l	24 1
11	14-MAR-2014	Blood creatine phosphokinase MB	14 IU/l	24 1
12	17-MAR-2014	Blood creatine phosphokinase MB	17 IU/l	24 1
13	07-SEP-2015	Blood iron	34, MCG/DL	193 33
14	05-OCT-2015	Blood iron	32, MCG/DL	193 33
15	05-OCT-2015	Blood iron	36, MCG/DL	193 33
16	13-MAR-2014	Blood triglycerides	97 mg/dl	200 1
17	26-AUG-2015	Cardiovascular examination	Pure and rhythmic, 4/6 holosystolic, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
18		Chest X-ray	no evidence of infiltrate or effusion, Unknown	
19		Chest X-ray	Pacemaker on right w/ atrial-ventricular probe, U	
20		Chest X-ray	Slight hypoventilation in left mid-field, Unknown	
21		Chest X-ray	status post partial lung resection, Unknown	
22		Chest X-ray	Borderline large heart, Unknown	
23		Chest X-ray	No definite signs of congestion, Unknown	
24		Chest X-ray	otherwise staple seam in right upper lung field,	
25		Chest X-ray	Sternotomy after cardiac surgery, Unknown	
26	28-AUG-2015	Colonoscopy	Massive residual contamination with a polyp bud, U	
27	28-AUG-2015	Colonoscopy	in the transversum, Unknown	
28	13-MAR-2014	Electrocardiogram	SM-ECG, marked left axis deviation LBBB, Unknown	
29	13-MAR-2014	Electrocardiogram	ST(-T)-segment changes caused by block, Unknown	
30	13-MAR-2014	Electrocardiogram	HR 72/min, S to V6, Unknown	
31	26-AUG-2015	Electrocardiogram	Indifference type, Unknown	
32	27-AUG-2015	Endoscopy upper gastrointestinal tract	Erythematous antral gastritis, Unknown	
33	27-AUG-2015	Endoscopy upper gastrointestinal tract	two angiodysplasia in in the proximal corpus, Unk	
34	27-AUG-2015	Endoscopy upper gastrointestinal tract	large curvature side, Unknown	
35	07-SEP-2015	Eosinophil count	3.6 %	6.0 1.0
36	05-OCT-2015	Eosinophil count	6 %	6.0 1.0
37	26-AUG-2015	Gastrointestinal examination	Soft, no pressure pain, no muscular defence, Unkn	
38	26-AUG-2015	Gastrointestinal examination	peristaltic, regular, Unknown	
39	01-AUG-2015	Haematocrit	27.9 %	47 37
40	13-AUG-2015	Haematocrit	25.7 %	44.9 34.1
41	18-AUG-2015	Haematocrit	26.4 %	44.9 34.1

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
42	24-AUG-2015	Haematocrit	27 %	44.9 34.1
43	02-SEP-2015	Haematocrit	28 %	44.9 34.1
44	07-SEP-2015	Haematocrit	26.2 %	44.9 34.1
45	14-SEP-2015	Haematocrit	36.4 %	44.9 34.1
46	05-OCT-2015	Haematocrit	34.7 %	44.9 34.1
47	01-JAN-2015	Haemoglobin	7.8 g/dl	
48	01-JAN-2015	Haemoglobin	7.5 g/dl	
49	01-JUL-2015	Haemoglobin	Decreased several points, Unknown	
50	01-AUG-2015	Haemoglobin	9.1 g/dl	16.0 12.0
51	13-AUG-2015	Haemoglobin	8.3 g/dl	15.7 11.2
52	18-AUG-2015	Haemoglobin	8.8 g/dl	15.7 11.2
53	07-SEP-2015	Haemoglobin	8.6 g/dl	15.7 11.2
54	14-SEP-2015	Haemoglobin	11.9 g/dl	15.7 11.2
55	05-OCT-2015	Haemoglobin	11.4 g/dl	15.7 11.2
56	26-AUG-2015	Heart rate	Normal, Unknown	
57	27-AUG-2015	Histology	Slight active gastritis of the reactive type, Unkn	
58	27-AUG-2015	Histology	no indication of malignancy, Unknown	
59	13-MAR-2014	International normalised ratio	1.76, Unknown	1.27 0.86
60	14-MAR-2014	International normalised ratio	2.04, Unknown	1.27 0.86
61	17-MAR-2014	International normalised ratio	2.08, Unknown	1.27 0.86
62	07-SEP-2015	Lymphocyte count	17.1 %	52.0 19.0
63	05-OCT-2015	Lymphocyte count	15.7 %	52.0 19.0
64	01-AUG-2015	Mean cell haemoglobin	33 pg	34 28
65	13-AUG-2015	Mean cell haemoglobin	31.8 pg	32.2 25.6
66	18-AUG-2015	Mean cell haemoglobin	33.3 pg	32.2 25.6
67	07-SEP-2015	Mean cell haemoglobin	32.5 pg	32.2 25.6

Mfr. Control Number: 2294363

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
68	14-SEP-2015	Mean cell haemoglobin	31.6 pg	32.2 25.6
69	05-OCT-2015	Mean cell haemoglobin	31.4 pg	32.2 25.6
70	01-AUG-2015	Mean cell haemoglobin concentration	33 g/dl	36 32
71	13-AUG-2015	Mean cell haemoglobin concentration	32.3 g/dl	36.0 32.0
72	18-AUG-2015	Mean cell haemoglobin concentration	33.3 g/dl	36.0 32.0
73	07-SEP-2015	Mean cell haemoglobin concentration	32.8 g/dl	36.0 32.0
74	14-SEP-2015	Mean cell haemoglobin concentration	32.7 g/dl	36.0 32.0
75	05-OCT-2015	Mean cell haemoglobin concentration	32.9 g/dl	36.0 32.0
76	01-AUG-2015	Mean cell volume	101.1, FL	94 80
77	13-AUG-2015	Mean cell volume	98.5, FL	94.8 79.4
78	18-AUG-2015	Mean cell volume	100, FL	94.8 79.4
79	07-SEP-2015	Mean cell volume	98.9, FL	94.8 79.4
80	14-SEP-2015	Mean cell volume	96.8, FL	94.8 79.4
81	05-OCT-2015	Mean cell volume	95.6, FL	94.8 79.4
82	07-SEP-2015	Monocyte count	13.3 %	13.0 5.0
83	05-OCT-2015	Monocyte count	11.5 %	13.0 5.0
84		Neurological examination	no abnormalities, Unknown	
85	26-AUG-2015	Neurological examination	Normal, Unknown	
86	07-SEP-2015	Neutrophil count	65.2 %	71.0 34.0
87	05-OCT-2015	Neutrophil count	66 %	71.0 34.0
88		Occult blood	Negative, Unknown	
89		Physical examination	reduced overall condition, Unknown	
90		Physical examination	no muscular guarding; peristalis was normal,Unkno	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
91		Physical examination	reduced adipose nutritional status, Unknown	
92		Physical examination	soft, no pain on palpation, Unknown	
93		Physical examination	rhythmic, Unknown	
94		Physical examination	non-irritated, Unknown	
95		Physical examination	vesicular breath sounds on both sides, Unknown	
96		Physical examination	no crepitations, no wheezing, no stridor, Unknown	
97	26-AUG-2015	Physical examination	Free of oedema, Unknown	
98	26-AUG-2015	Physical examination	No pressure pain in the calf, Unknown	
99	26-AUG-2015	Physical examination	Free, Unknown	
100	26-AUG-2015	Physical examination	awake and oriented to person, place and time, Unk	
101	26-AUG-2015	Physical examination	Stable condition and good dietary status, Unknown	
102	26-AUG-2015	Physical examination	Without pain on percussion, Unknown	
103	01-AUG-2015	Platelet count	266, X10**3/MCL	400 140
104	13-AUG-2015	Platelet count	284/nl, Unknown	400 150
105	18-AUG-2015	Platelet count	306/nl, Unknown	400 150
106	07-SEP-2015	Platelet count	307/nl, Unknown	400 150
107	14-SEP-2015	Platelet count	317/nl, Unknown	400 150
108	05-OCT-2015	Platelet count	316/nl, Unknown	400 150
109	13-MAR-2014	Prothrombin time	41 %	130 82
110	14-MAR-2014	Prothrombin time	35 %	130 82
111	17-MAR-2014	Prothrombin time	35 %	130 82
112	26-AUG-2015	Pulmonary physical examination	Vesicular respiratory sound on both sides, Unknown	
113	26-AUG-2015	Pulmonary physical examination	no rattling sounds, Unknown	
114	01-AUG-2015	Red blood cell count	2.76, X10**6/MCL	6.1 4.6
115	13-AUG-2015	Red blood cell count	2.6/pl, Unknown	6.1

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				4.6
116	18-AUG-2015	Red blood cell count	2.6/pl, Unknown	6.1 4.6
117	07-SEP-2015	Red blood cell count	2.7/pl, Unknown	6.1 4.6
118	14-SEP-2015	Red blood cell count	3.8/pl, Unknown	6.1 4.6
119	05-OCT-2015	Red blood cell count	3.6/pl, Unknown	6.1 4.6
120	01-AUG-2015	Red cell distribution width	17.3 %	14.5 11.5
121		Respiratory rate	175/80 mmHg	
122		Respiratory rate	93 %	
123		Respiratory rate	63, Beats per minute	
124	26-AUG-2015	Respiratory rate	16, Unknown	
125		Stress echocardiogram	with formation of posterior wall aneurysm, Unknown	
126		Stress echocardiogram	no evidence of ischemia under stress criteria, Unk	
127		Stress echocardiogram	with s/p posterior wall infarction, Unknown	
128	13-MAR-2014	Troponin T	43, PG/ML	
129	13-MAR-2014	Troponin T	43, PG/ML	
130	01-AUG-2015	White blood cell count	7.5, X10**3/MCL	10.8 4.3
131	13-AUG-2015	White blood cell count	9.2/nl, Unknown	9.1 4.2
132	18-AUG-2015	White blood cell count	8.1/nl, Unknown	9.1 4.2
133	07-SEP-2015	White blood cell count	9.6/nl, Unknown	9.1 4.2
134	14-SEP-2015	White blood cell count	9.3/nl, Unknown	9.1 4.2
135	05-OCT-2015	White blood cell count	8.8/nl, Unknown	9.1 4.2

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 3E359F3; Exp.Dt. 01-AUG-2015}; Regimen #1	26 IU/kg/week, Freq: 2 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	22-OCT-2012 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 5O021Q5; Exp.Dt.	26 IU/kg/week, Freq: 2 Week; Interval: 1;	Renal anaemia (Nephrogenic anaemia)	22-OCT-2012 / Unknown;

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
01-AUG-2017}; Regimen #2	Subcutaneous		Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ATORVASTATIN (ATORVASTATIN) ; Unknown

#8) BISOPROLOL (BISOPROLOL) ; Unknown

#9) BONDIOL (ALFACALCIDOL) ; Unknown

#10) DEKRISTOL (COLECALCIFEROL) ; Unknown

#11) MIMPARA (CINACALCET HYDROCHLORIDE) ; Unknown

#12) RAMIPRIL (RAMIPRIL) ; Unknown

#13) TORASEMIDE (TORASEMIDE) ; Unknown

#14) XIPAMIDE (XIPAMIDE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption was not reported. The patient was not pregnant at the time of treatment and had no known drug hypersensitivities or history of drug dependence. Medical history included myocardial failure NYHA II, status post triple ACVB surgery (LIMA to RIVA, 2 ACVB to RCX and RPD May-1999), atrial fibrillation since 06-Aug-2005, DDDR pacemaker for post ablation of an isthmus-dependent atrial flutter in Mar-2010, severe stenosis of the aortic bifurcation with intermittent claudication IIb both sides, hyperlipidemia since 28-Jul-2010, peripheral arterial disease since 28-Jul-2010, diabetic nephropathy which led to the diagnosis of chronic dialysis-dependent kidney failure stage V, hypertensive nephrosclerosis (confirmed by histology Aug-2010), on hemodialysis 3 times per week since 26 Jul 2011, cancer since 30-Dec-2012, status post upper lobe resection in Jan-2013 for bronchial carcinoma (Tx, N0, M0), status post LAD-PTCA with implant of a DES (12-Dec-2013), 3-vessel coronary artery disease with non-invasive exclusion of a CHD progression in 18-Mar-2014, shunt insertion left cubital fossa, nephrotic and nephritic syndrome and secondary renal hyperparathyroidism. The patient had not been treated with other erythropoietin stimulating agents (ESA) and had no previous exposure to other biosimilars. Risk factors included coronary heart disease also reported as 3-vessel coronary artery disease, vascular anomalies, posterior myocardial infarction 1999 with aneurysm associated with posterolateral akinesia, end stage renal disease, ischemic heart disease since 02-Apr-2014, type 2 diabetes mellitus without vascular complications also reported as Type 2 diabetes mellitus, non-insulin-dependent since 27-Aug-2010, arterial hypertension, hyperlipoproteinaemia, and former nicotine abuse also reported as ex-smoker. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History 30-Dec-2012	Bronchial carcinoma (Bronchial carcinoma);
Unknown to Ongoing	Relevant Med History on Mar 2010	DDDR pacemaker for post ablation of an isthmus-dependent atrial flutter ();
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History 28-Jul-2010	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History confirmed by histology Aug 2010	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Kidney failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
Unknown to Ongoing	Relevant Med History	Nephrotic syndrome (Nephrotic syndrome);
Unknown to Ongoing	Relevant Med History	Nephritic syndrome (Nephritic syndrome);
Unknown to Ongoing	Relevant Med History 28-Jul-2010	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown to Ongoing	Relevant Med History	Stenosis aortic valve (Aortic valve stenosis);
Unknown	Relevant Med History 12-Dec-2013	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
Unknown	Relevant Med History	Posterior myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Stenosis aortic valve (Aortic valve stenosis);
Unknown	Relevant Med History	Cubital tunnel syndrome (Cubital tunnel syndrome);
Unknown	Relevant Med History May 1999	Coronary artery bypass (Coronary artery bypass);
Unknown	Relevant Med History 01/2013	Lung lobectomy (Lung lobectomy);
Unknown	Relevant Med History Risk Factor-18-Mar-2014	Coronary artery disease progression (Coronary artery disease);
Unknown	Relevant Med History Risk Factor-27-Aug-2010	Diabetes mellitus (Diabetes mellitus);
Unknown	Relevant Med History Risk Factor	End stage renal disease (ESRD) (End stage renal disease);
Unknown	Relevant Med History Risk Factor	Hyperlipoproteinemia (Hyperlipidaemia);
Unknown	Relevant Med History Risk Factor	Hypertension arterial (Hypertension);
Unknown	Relevant Med History Risk Factor-02-Apr-2014	Ischemic heart disease (Myocardial ischaemia);

Mfr. Control Number: 2294363

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History Risk Factor	Nicotine abuse (Tobacco abuse);
Unknown	Relevant Med History Risk Factor-1999	Posterior myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History Risk Factor	Anomalies congenital multiple (Multiple congenital abnormalities);
Unknown	Relevant Med History Risk Factor-on Mar 2010	Pacemaker insertion (cardiac) (Cardiac pacemaker insertion);
Unknown	Relevant Med History Risk Factor-since 26-Jul-2011	Hemodialysis (Haemodialysis);
Unknown	Past Drug Event	MARCUMAR (MARCUMAR); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
Unknown	Past Drug Event	ANTIBIOTIC /00011701 (ANTIBIOTIC /00011701/); Drug Indication: Flu-like illness (Influenza like illness)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	FINLAND	08	MAR	1936	78 Years	Male	80.00 kg	28	APR	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischemic stroke [Ischaemic stroke]

Case Description: Ischemic stroke. Epoetin zeta. Serious Hospira-sponsored study report from Finland, received from an investigator (reference: Fin-002-0003), which refers to a 78-year-old male patient (weight: 80 kg; height: 176 cm). The patient was
enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included hyperlipidemia in 2000 with LDL

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 6000 IU, Freq: 1 Week, Interval:1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-MAR-2014 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL (ALLOPURINOL) ; 01-JAN-2000 / Unknown
#2) AMLODIPINE (AMLODIPINE) ; 01-JAN-2000 / Unknown
#3) ASA (ACETYLSALICYLIC ACID) ; 01-JAN-2010 / Unknown
#4) BISOPROLOL (BISOPROLOL) ; 01-JAN-2000 / Unknown
#5) FUROSEMIDE (FUROSEMIDE) ; 01-JAN-2000 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Cerebrovascular disorder (Cerebrovascular disorder)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2335062

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

of 3.1 mmol/L, peripheral arterial disease in 2010, cerebrovascular disease, hypertension since 2010, and hypertensive nephropathy leading to renal failure on 12-Mar-2002. The patient was not at any time exposed to any other erythropoietin-stimulating agent (ESA) before treatment with Retacrit. The patient did not have any previous exposure to other biosimilar products. Concomitant medications included amlodipine (5 mg, once a day) for hypertension, bisoprolol (5 mg, once a day) for an unknown indication, furosemide (40 mg, twice a day) for an unknown indication, allopurinol (100 mg, once a day) for gout and ASA (100 mg, once a day) for an unknown indication. On 12-Mar-2014, the patient started treatment with epoetin zeta (Retacrit, 6,000 IU, once every week, subcutaneous; batch number unknown) for renal anaemia. On 28-Apr-2014, the patient experienced ischemic stroke and was hospitalised. It was reported that the patient felt fatigue and was unconscious. He had developed left side hemiplegy and convulsions. On 28-Apr-2014 at 15:31, laboratory tests included CRP 11 mg/L (normal values: 0-8), leukocytes 9.4 (unit not reported; normal values: 3.4-8.2), erythrocytes 3.17 (unit not reported; normal values: 4.25-5.70), haemoglobin 100 (unit not reported; normal values: 134-167), haematocrit 0.31 (unit not reported; normal values: 0.39-0.50), thrombocytes 158 x E9/l (normal values: 150-360), APTT 24 s (normal values: 24-35), and INR 1.0 (normal values: 2.0-3.0), and CK 74 U/L (normal values: 40-280). On 29-Apr-2014 at 07:00, investigations revealed leukocytes 12.5, erythrocytes 3.42, haemoglobin 107, haematocrit 0.34, and thrombocytes 180 E9/L. On 30-Apr-2014 at 07:00, laboratory tests included CRP 99 mg/L, leukocytes 8.7, erythrocytes 3.12, haemoglobin 97, haematocrit 0.31, and thrombocytes 154 E9/L. On 01-May-2014 at 07:00, laboratory tests included CRP 111 mg/L, leukocytes 10.0, erythrocytes 3.33, haemoglobin 104, haematocrit 0.33, and thrombocytes 156 E9/L. On 02-May-2014 at 07:00, laboratory tests included CRP 94 mg/L, leukocytes 6.1, erythrocytes 3.07, haemoglobin 96, haematocrit 0.30, and thrombocytes 158 E9/L. Treatment for the adverse events included enoxaparin and fenytoin (dose and route of administration not reported). No action was taken with Retacrit. The patient recovered from the adverse event on an unknown date. On 19-Apr-2015, the patient died. Cause of death was pneumonia. It was not reported if autopsy was performed. The reporter's causality assessment between the event of ischemic stroke and epoetin zeta was possible. 22-May-2014: Additional information was received from the same reporter that the patient did not have any previous exposure to other biosimilar products. No action was taken with Retacrit. Treatment for the adverse event also included fenytoin (previously reported as illegible). The patient recovered from the adverse event on an unknown date. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. This information has been incorporated in the narrative and in the corresponding data fields. 21-Apr-2015: Additional information was received from the same reporter that the patient died on 19-Apr-2015, cause of death was pneumonia. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Noting that the patient has received the suspect drug for more than a month and that any increase in red blood cell concentration can theoretically increase the risk of thromboembolic and ischemic events, cannot totally rule out possible contributory effect from the suspect drug. Consider also contributory effects of pre-existing and predisposing risk factors for ischemia. Follow-up: No change in previous causality assessment. Follow-up: Overall case causality: Related New information noted. Causality updated from possible to related in accordance with company's new binary causality assessment. Suspect drug can theoretically increase the risk of thromboembolic events.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	28-APR-2014	Activated partial thromboplastin time	24 seconds	35 24
2	28-APR-2014	Blood creatine phosphokinase	74 IU/l	280 40
3	28-APR-2014	C-reactive protein	11 mg/l	8 0
4	30-APR-2014	C-reactive protein	99 mg/l	8 0
5	01-MAY-2014	C-reactive protein	111 mg/l	8 0
6	02-MAY-2014	C-reactive protein	94 mg/l	8 0
7	28-APR-2014	Haematocrit	0.31, Unknown	0.50 0.39
8	29-APR-2014	Haematocrit	0.34 ,Unknown	0.50 0.39
9	30-APR-2014	Haematocrit	0.31, Unknown	0.50 0.39

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
10	01-MAY-2014	Haematocrit	0.33, Unknown	0.50 0.39
11	02-MAY-2014	Haematocrit	0.30 ,Unknown	0.50 0.39
12	28-APR-2014	Haemoglobin	100, Unknown	167 134
13	29-APR-2014	Haemoglobin	107, Unknown	167 134
14	30-APR-2014	Haemoglobin	97, Unknown	167 134
15	01-MAY-2014	Haemoglobin	104, Unknown	167 134
16	02-MAY-2014	Haemoglobin	96, Unknown	167 134
17	28-APR-2014	International normalised ratio	1.0, Unknown	3.0 2.0
18	28-APR-2014	Platelet count	158 x10 9/l	360 150
19	29-APR-2014	Platelet count	180 x10 9/l	360 150
20	30-APR-2014	Platelet count	154 x10 9/l	360 150
21	01-MAY-2014	Platelet count	156 x10 9/l	360 150
22	02-MAY-2014	Platelet count	158 x10 9/l	360 150
23	28-APR-2014	Red blood cell count	3.17, Unknown	5.70 4.25
24	29-APR-2014	Red blood cell count	3.42, Unknown	5.70 4.25
25	30-APR-2014	Red blood cell count	3.12, Unknown	5.70 4.25
26	01-MAY-2014	Red blood cell count	3.33, Unknown	5.70 4.25
27	02-MAY-2014	Red blood cell count	3.07, Unknown	5.70 4.25
28	28-APR-2014	White blood cell count	9.4, Unknown	8.2 3.4
29	29-APR-2014	White blood cell count	12.5, Unknown	8.2 3.4
30	30-APR-2014	White blood cell count	8.7, Unknown	8.2 3.4
31	01-MAY-2014	White blood cell count	10.0, Unknown	8.2 3.4
32	02-MAY-2014	White blood cell count	6.1, Unknown	8.2 3.4

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();

Allergies and alcohol consumption were not reported. Medical history included hyperlipidemia

Mfr. Control Number: 2335062

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		in 2000 with LDL of 3.1 mmol/L, peripheral arterial disease in 2010, cerebrovascular disease, hypertension since 2010, and hypertensive nephropathy leading to renal failure on 12-Mar-2002. The patient was not at any time exposed to any other erythropoietin-stimulating agent (ESA) before treatment with Retacrit. The patient did not have any previous exposure to other biosimilar products. Race/ethnicity: Caucasian The patient died on 19-Apr-2015. Cause of death was pneumonia.
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia); since 2000; LDL 3.1 mmol/L
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension); since 2000
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease); since 2010
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	15	SEP	1952	Unk	Male	100.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Thromboembolic events [Embolism]

Case Description: This report was entered as a result of retrospective remediation following an MHRA inspection regarding seriousness assessment in relation to the MedDRA IME list, which has now been incorporated in case processing. This is a Hospira-
Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 120 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 22-OCT-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2481084

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-AUG-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2481084

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This report describes a case of thromboembolic events. This serious case from an investigator (It-022-0018) describes a male patient (age not reported; weight: 100 kg and height: 172 cm) who received Retacrit (epoetin zeta; 120 IU/kg/week, 3 dosage/week, subcutaneous, batch number not reported) for renal anaemia from 22-Oct-2013. Medical history included diabetic nephropathy that led to renal failure diagnosed on 22-Oct-2013. It was also reported that the patient was on dialysis since 13-Dec-2013. Concomitant medications were not reported. On 22-Oct-2013, the patient began treatment with epoetin zeta. However, it was reported that the patient signed the informed consent on 17-Dec-2013. On an unknown date, the patient developed thromboembolic events. Treatment for, action taken with the suspect drug, and outcome of the adverse event were not reported. The reporter's causality assessment for the event of thromboembolic events in relation to epoetin zeta was not reported. Risk factors included myocardial infarction, peripheral arterial disease, hyperlipidaemia, diabetes type II, and heart failure NYHA stage III. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure of patient to other biosimilar products. 08-Jun-2015: Corrected report was created to update the seriousness criteria to serious (medically significant). This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Though the patient has significant risk factors in the medical history which increases the risk for ischemia, Retacrit can also theoretically increase the risk of thromboembolic events by increasing red blood cell concentration. Corrected report: Case corrected to upgrade seriousness, but does not warrant change in previous causality assessment.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	120 IU/kg, Freq: 1 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	22-OCT-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included diabetic nephropathy that led to renal failure diagnosed on 22-Oct-2013. It was also reported that the patient was on dialysis since 13-Dec-2013. Risk factors included myocardial infarction, peripheral arterial disease, hyperlipidaemia, diabetes type II, and heart failure NYHA stage III. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown	Relevant Med History 13-Dec-2013	Dialysis (Dialysis);
Unknown	Relevant Med History	Type II diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	03	FEB	1938	76 Years	Female	61.00 kg	12	MAY	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMIACS [Acute myocardial infarction]

Case Description: NSTEMI-ACS. Epoetin zeta. Serious Hospira sponsored study report from Italy, received from an investigator (reference: It-022-0015), which refers to a 76-year-old Caucasian female patient (height: 152 cm, dry weight: 61 kg). This
patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient was an ex-smoker who started in

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 103 IU/kg/ (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 14-FEB-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CARDICOR (BISOPROLOL FUMARATE) ; 02-APR-2013 / Unknown
#2) FOZNOL (LANTHANUM CARBONATE) ; 16-NOV-2013 / Unknown
#3) LASIX /00032601/ (FUROSEMIDE) ; Unknown
#4) MIMPARA (CINACALCET HYDROCHLORIDE) ; 13-FEB-2014 / Unknown
#5) ASA (ACETYLSALICYLIC ACID) ; Unknown
#6) MAGNESIUM CARBONATE (MAGNESIUM CARBONATE) ; 29-MAR-2013 / Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Diagnosed on 05-Feb-2013	Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2519067

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-MAR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

1986 until 1996 with 10 cigarettes/day. The patient had an unknown diagnosis which led to renal failure diagnosed on 05-Feb-2013. The patient was on dialysis since 05-Feb-2013 with an average frequency of 3 per week. The patient did not receive Retacrit prior to the study. No other EPO or biosimilar was used before Retacrit. The patient was not pregnant and not lactating. Concomitant medications included Cardicor 2.5 mg (1 tablet, morning) for heart failure, Foznol (1500 mg, twice) and magnesium carbonate (1600 mg, twice also reported as 2 tablets x 2 in the morning and evening) for blood phosphorus increased; omeprazole (20 [unit of measurement not reported], once) for uremic gastritis, Mimpara (30 mg, once) for hyperparathyroidism secondary, and sodium bicarbonate 500 mg (2 'fi', twice also reported as 2 tablets x 2 in the morning and evening) for metabolic acidosis; ASA 100 mg (acetylsalicylic acid; 1 tablet), Lasix 25 mg (2 tablets x 2, morning and early afternoon), and pantoprazole 20 mg (1 tablet, morning) for an unknown indications; routes of administration not reported. On 14-Feb-2013, the patient started treatment with Retacrit (epoetin zeta; 103 IU/kg/week, 3 dosages per week, subcutaneous; batch number unknown) for renal anemia. It was reported that on 10-May-2014, the patient received last dose prior to the event. On 12-May-2014, the day before admission, the patient experienced onset of chest pain during a session of dialysis. It was reported that the patient experienced precordial pain during dialysis treatment and elevated troponin I. On 13-May-2014, the patient was admitted and was diagnosed with NSTEMI-ACS. At the time of admission, a cardiology assessment revealed dilation of the left ventricle with reduced overall contractility and moderate mitral insufficiency. During hospitalisation, several tests were carried out including the following: Maximum TnI peak=5.77; CK-Mass=13.3 (unit of measurement and normal range not reported). Mild dyslipidaemia was also noted with total cholesterol=212, LDL=136, HDL=53 and triglycerides=115. Admission ECG was also done and showed SR at HR 90; normal AV conduction, Q-wave in D3 and aVF and T-wave negative in D1, aVL and from V4 to V6. On the same day of 13-May-2014, chest x-ray was performed in a supine position and only in AP projection and showed an enlarged cardiac silhouette with signs of interstitial-alveolar oedema, aortosclerosis, no pleural effusion. On 14-May-2015 at 06:35, CK-MB mass was at 9.20 ng/ml (normal range: 0.50-3.60) and troponin I was at 5.770 ng/ml (normal range: 0.000-0.045). On 16-May-2014, coronary angiography was done and showed 3-vessel disease, extended coronary calcification. On the same day, echocardiogram was done and revealed left ventricle of normal intracavitary dimensions with hypertrophy of the IVS. Hypokinesis of the mediobasal lateral wall, hypokinesis of the medial inferior wall and akinesia of the basal segment of the inferior wall. Overall contractile function of the left ventricle at the lower limits. Aneurism of the interatrial septum with two-directional movement in absence of evident shunt in basal conditions. Aortic root at the upper limits, ascending aorta and arc within the normal limits of their dimensions and aspect. Isthmic flow normal. Aortosclerosis of the tricuspid aortic valve, scleral calcification with anterograde gradients indicating mild stenosis (max pressure gradient 20 mmHg, average 11 mmHg), moderate aortic insufficiency. Left atrium at the upper limits. Calcification of the posterior mitral annulus. Mitral valve apparatus fibrosclerotic with moderate insufficiency with an eccentric jet directed towards the lateral wall of the atrium. Transmitral Doppler pattern from abnormal diastolic relation. Right sections not dilated. VCI not dilated with preserved respiratory excursions. Minimal tricuspid valve insufficiency with PAPs within the normal limits. Pericardium intact. On 19-May-2014, echo doppler showed moderate ATS with no significant stenosis. On the same day, pulmonary tests at the lower limits of the normal range showed slight reduction in pulmonary volumes indicating mild restrictive syndrome. On an unknown date, chest CT-scan was performed exclusively in baseline conditions and showed aortic root at upper limits, ascending aorta, arc and descending aorta within normal limits for dimensions, with diffuse parietal calcification also involving the origin-tract, proximal tract of the epiaortic vessels. Calcification of the aortic and mitral valve, extended coronary calcification with dilation of the left ventricle. On 24-May-2014, ECG showed SR substantially unchanged. It was also reported that the patient was currently asymptomatic and in good haemodynamic compensation. The patient was advised to continue with the home treatment ASA, magnesium carbonate, sodium bicarbonate, Lasix, pantoprazole, and Cardicor. It was also reported that in relation to the forthcoming heart surgery, dual antiplatelet therapy has not been established, therefore, if the same is not carried out, it was advised to add Plavix 75 mg, 1 tablet in the morning. Treatment for the event, and action taken with epoetin zeta in response to the adverse event were not reported. Outcome of the event was recovered on an unknown date and the patient was discharged on 24-May-2014. The reporter's causality assessment for the event of NSTEMI-ACS in relation to epoetin zeta was not related. Risk factors included hypertension since 1996 and smoking. 11-Mar-2015: Additional information was received from the investigator. The reporter was able to provide the following information for the identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. This information has been reflected in the narrative. 24-Mar-2015: Additional information was received from the investigator. Follow up report was created to reflect the patient's age; details of smoking history was provided, height and weight were updated, and concomitant medications were added. The adverse event was updated to NSTEMI-ACS (previously reported as thromboembolic events); details of the event, outcome, laboratory, diagnostic tests, and reporter's causality assessment were also updated. Start date of hypertension was provided and seriousness criterion was changed to hospitalization. It was reported that on 10-May-2014, the patient received last dose prior to the event. This information has been reflected in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and date of expiry.

Case Comment: Overall case causality: Possible Although there are reported cardiovascular risk factors (hypertension and smoking), event is still possibly related to the suspect drug. Retacrit can theoretically increase the risk of thromboembolic events by increasing red blood cell concentration. Limited information makes it difficult to provide a more definitive assessment. - N. Gonzales (05 Sep 2014) Follow-up: New information noted. Company causality also updated to not assessable - Cannot provide causation of event without firm timeline of occurrence of the adverse event, as well as further objective clinical event details. - N. Gonzales (19 Mar 2015) Follow-up: New information noted, including updated timelines,

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

more detailed medical history and reportet's causality assessment. Company causality changed to not related. The cardiovascular risk factors which were present for almost two decades outweigh the potential rsik from the suspect drug. - N. Gonzales (30 Mar 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	16-MAY-2014	Angiogram	3-vessel disease, extended coronary calcification	
2	13-MAY-2014	Blood cholesterol	212, Unknown	
3	13-MAY-2014	Blood creatine phosphokinase MB	13.3, Unknown	
4	14-MAY-2014	Blood creatine phosphokinase MB	9.20 ng/ml	3.60 0.50
5	13-MAY-2014	Blood triglycerides	115, Unknown	
6	13-MAY-2014	Chest X-ray	aortosclerosis, no pleural effusion, Unknown	
7	13-MAY-2014	Chest X-ray	interstitial-alveolar oedema, Unknown	
8	13-MAY-2014	Chest X-ray	Enlarged cardiac silhouette with signs of,Unknown	
9		Computerised tomogram thorax	with dilation of the left ventricle,Unknown	
10		Computerised tomogram thorax	aortic root at upper limits, ascending aorta,Unkn	
11		Computerised tomogram thorax	proximal tract of the epiaortic vessels, Unknown	
12		Computerised tomogram thorax	within normal limits for dimensions, Unknown	
13		Computerised tomogram thorax	arc and descending aorta, Unknown	
14		Computerised tomogram thorax	also involving the origin-tract,Unknown	
15		Computerised tomogram thorax	with diffuse parietal calcification,Unknown	
16		Computerised tomogram thorax	extended coronary calcification,Unknown	
17		Computerised tomogram thorax	Calcification of the aortic and mitral valve, Unk	
18	16-MAY-2014	Echocardiogram	Minimal tricuspid valve insufficiency with PAPs,U	
19	16-MAY-2014	Echocardiogram	moderate aortic insufficiency,Unknown	
20	16-MAY-2014	Echocardiogram	Aortosclerosis of the tricuspid aortic valve, Unk	
21	16-MAY-2014	Echocardiogram	ascending aorta and arc within, Unknown	
22	16-MAY-2014	Echocardiogram	Calcification of the posterior mitral annulus, Un	
23	16-MAY-2014	Echocardiogram	directional movement in	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			absence of evident,Unknow	
24	16-MAY-2014	Echocardiogram	hypokinesis of the medial inferior wall,Unknown	
25	16-MAY-2014	Echocardiogram	Hypokinesis of the mediobasal lateral wall,Unknow	
26	16-MAY-2014	Echocardiogram	Left atrium at the upper limits,Unknown	
27	16-MAY-2014	Echocardiogram	left ventricle at the lower limits,Unknown	
28	16-MAY-2014	Echocardiogram	Mitral valve apparatus fibrosclerotic with,Unknown	
29	16-MAY-2014	Echocardiogram	directed towards the lateral wall of the atrium, U	
30	16-MAY-2014	Echocardiogram	with preserved respiratory excursions,Unknown	
31	16-MAY-2014	Echocardiogram	Overall contractile function of the,Unknown	
32	16-MAY-2014	Echocardiogram	Right sections not dilated,Unknown	
33	16-MAY-2014	Echocardiogram	scleral calcification with anterograde gradients,	
34	16-MAY-2014	Echocardiogram	shunt in basal conditions,Unknown	
35	16-MAY-2014	Echocardiogram	the normal limits of their dimensions and aspect,U	
36	16-MAY-2014	Echocardiogram	Transmitral Doppler pattern from,Unknown	
37	16-MAY-2014	Echocardiogram	VCI not dilated, Unknown	
38	16-MAY-2014	Echocardiogram	with hypertrophy of the IVS, Unknown	
39	16-MAY-2014	Echocardiogram	abnormal diastolic relation, Unknown	
40	16-MAY-2014	Echocardiogram	within the normal limits. Pericardium intact, Unk	
41	16-MAY-2014	Echocardiogram	akinesia of the basal segment of the inferior wal	
42	16-MAY-2014	Echocardiogram	Aortic root at the upper limits,Unknown	
43	16-MAY-2014	Echocardiogram	left ventricle of normal intracavitary dimensions,	
44	16-MAY-2014	Echocardiogram	moderate insufficiency with an eccentric jet,Unkno	
45	16-MAY-2014	Echocardiogram	(max pressure gradient 20 mmHg,average 11 mmHg),Un	
46	16-MAY-2014	Echocardiogram	Isthmic flow normal, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
47	16-MAY-2014	Echocardiogram	gradients indicating mild stenosis, Unknown	
48	16-MAY-2014	Echocardiogram	Aneurism of the interatrial septum with two,Unkno	
49	19-MAY-2014	Echocardiogram	Moderate ATS with no significant stenosis,Unknow	
50	13-MAY-2014	Electrocardiogram	SR at HR 90; normal AV conduction, Unknown	
51	13-MAY-2014	Electrocardiogram	Q-wave in D3 and aVF and T-wave negative in D1,Un	
52	13-MAY-2014	Electrocardiogram	aVL and from V4 to V6, Unknown	
53	24-MAY-2014	Electrocardiogram	SR substantially unchanged,Unknown	
54	13-MAY-2014	High density lipoprotein	53, Unknown	
55	13-MAY-2014	Low density lipoprotein	136, Unknown	
56	19-MAY-2014	Pulmonary function test	indicating mild restrictive syndrome,Unknown	
57	19-MAY-2014	Pulmonary function test	Slight reduction in pulmonary volumes,Unknown	
58	12-MAY-2014	Troponin I	Elevated, Unknown	
59	13-MAY-2014	Troponin I	5.77, Unknown	
60	14-MAY-2014	Troponin I	5.770 ng/ml	0.045 0.000

13. Relevant Tests

Chest CT-scan : aortic root at upper limits, ascending aorta, Unknown
Chest CT-scan : Calcification of the aortic and mitral valve, Unknown
Coronary angiography (16-May-2014) : 3-vessel disease, extended coronary calcification, Unknown
ECG (13-May-2014) : Q-wave in D3 and aVF and T-wave negative in D1, Unknown
Echocardiogram (16-May-2014) : akinesia of the basal segment of the inferior wall, Unknown
Echocardiogram (16-May-2014) : Aneurism of the interatrial septum with two, Unknown
Echocardiogram (16-May-2014) : Aortosclerosis of the tricuspid aortic valve, Unknown
Echocardiogram (16-May-2014) : Calcification of the posterior mitral annulus, Unknown
Echocardiogram (16-May-2014) : directed towards the lateral wall of the atrium , Unknown
Echocardiogram (16-May-2014) : directional movement in absence of evident, Unknown
Echocardiogram (16-May-2014) : Hypokinesis of the mediobasal lateral wall, Unknown
Echocardiogram (16-May-2014) : left ventricle of normal intracavitary dimensions, Unknown
Echocardiogram (16-May-2014) : (max pressure gradient 20 mmHg, average 11 mmHg), Unknown
Echocardiogram (16-May-2014) : Minimal tricuspid valve insufficiency with PAPs, Unknown
Echocardiogram (16-May-2014) : moderate insufficiency with an eccentric jet, Unknown
Echocardiogram (16-May-2014) : scleral calcification with anterograde gradients, Unknown
Echocardiogram (16-May-2014) : the normal limits of their dimensions and aspect, Unknown
Echocardiogram (16-May-2014) : within the normal limits. Pericardium intact, Unknown
Echo doppler (19-May-2014) : Moderate ATS with no significant stenosis, Unknown

14-19. SUSPECT DRUG(S) continued

Mfr. Control Number: 2519067

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	103 IU/kg/week, Freq: 3 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	14-FEB-2013 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) OMEPRAZOLE (OMEPRAZOLE) ; 25-MAY-2013 / Unknown

#8) PANTOPRAZOLE (PANTOPRAZOLE) ; Unknown

#9) SODIUM BICARBONATE (SODIUM BICARBONATE) ; 07-SEP-2013 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); The patient was an ex-smoker who started in 1986 until 1996 with 10 cigarettes/day. The patient had an unknown diagnosis which led to renal failure diagnosed on 05-Feb-2013. The patient was on dialysis since 05-Feb-2013 with an average frequency of 3 per week. The patient did not receive Retacrit prior to the study. No other EPO or biosimilar was used before Retacrit. The patient was not pregnant and not lactating. Risk factors included hypertension and smoking. Race/Ethnicity: Caucasian.
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Tobacco user (Tobacco user);
Unknown	Relevant Med History	Dialysis (Dialysis);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	01	JAN	1933	79 Years	Male	65.00 kg	11	OCT	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: NSTEMI. Epoetin zeta. Serious Hospira sponsored clinical study report from Germany, received from an investigator (reference: Ge-117-0009), which refers to a 79-year old Caucasian male patient (height: 172 cm, dry weight: 65 kg).
The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history included

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 92 IU/kg, Freq: 1 week, Interval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 16-APR-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMPHO-MORONAL (AMPHOTERICIN B) ; Unknown
#2) ASS (ACETYLSALICYLIC ACID) ; Unknown
#3) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCC
#4) BIFITERAL (LACTULOSE) ; Unknown
#5) DECORTIN (PREDNISONE) ; Unknown
#6) DIGIMERCK (DIGITOXIN) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Arteriosclerosis (Arteriosclerosis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2562115

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-FEB-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

thromboendarterectomy of the left internal carotid artery in 1998, quadruple aortocoronary venous bypass (AVCB) carried out in Apr-2003, occlusion of the right cardiac artery (RCA), severe stenosis of RIVA and RCX, LIMA on RIVA, mild aortic insufficiency, abdominal aortic aneurysm (not more than 4 cm in width), pulmonary emphysema with stage II COPD treated with oxygen therapy, benign prostatic hyperplasia, vocal cord paresis (left side), post-status abdominal wall haematoma during Arixtra administration, TAA status post atrial thrombus in July-2009, heparin-induced thrombocytopenia, myelodysplastic syndrome with anaemia treated with 4 red cell concentrate transfusions, post-status amiodaroneinduced hypothyroidism, left side ischemic heart disease, peripheral arterial disease with the disobliteration of the left femoral artery in Mar-2012, atrial fibrillation; and arteriosclerosis which led to renal failure diagnosed in Jan-2011. The patient had status post left cardiac catheterisation on 08-Oct-2012. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the study. The patient was not treated with an ESA before treatment with Retacrit.
The patient had no previous exposure to other biosimilars. Concomitant medications included Xarelto (15 mg, 1-0-0), Bifiteral (10 ml, 1-1-1); Torem 10 (1-0-0), ASS 100 (discontinued for the time being), Belok Zok (1-0-0), Decortin 15 (1-0-0), Xipamid 10 (1-0-0), Digimerk 0.07 (1-0-0), Mst 10 (0-0-1), Pantozol 40 (1-0-0), Ranexa 375 (1-0-1), Ampho-Moronal (1-1-1-1) (doses and routes of administration not reported); Oxis (1-0-1, inhalation) and Spiriva (1-0-0, inhalation); all given for unknown indications. On 18-Apr-2011, the patient started treatment with Retacrit (epoetin zeta, 92 IU/kg/week, first dose also reported as 6000, unit not reported; 1 dosage/week, subcutaneous, batch number unknown) for renal anaemia. It was reported that dose of Retacrit prior to the event was 10,000 (unit of measurement not reported). On 11-Oct-2012, the patient experienced NSTEMI with moderate shortness of breath, described as chest pain. It was reported that the patient was admitted to a hospital for further monitoring NSTEMI during three-vessel coronary artery disease from 11 to 25-Oct-2012. Physical examination was performed and showed that the patient's general/dietary condition was normal. The patient was aware and oriented, nothing abnormal was detected in the skin or mucous membranes; no foetor or oedemas; head and neck status age-appropriate; no dyspnoea. Lungs: vesicular breath sounds bilaterally, no crackles. Heart: clear and arrhythmic, no cardiac murmurs. Abdomen: soft, no tenderness on palpation, no guarding/rebound. Peristaltic sounds normal. No throbbing pain in the renal capsule. Free movement of the extremities. No evidence of fresh neurological deficits. On 11-Oct-12012, ECG was done and showed AA at normal heart rate, negative T wave in leads I, II and III, aVF, v4-v6. On an unknown date, a prolonged ECG with a 22-hour recording of a satisfactory quality was performed and showed continuous AA in VHF, HF 73 beats/min, minimum 65 beats/min, maximum 114 beats/min, maximum RR distance 1.9 sec, 49 polymorphic VES, isolated couplets, prolonged RR: normal in the centre, low to normal values at night, with good RR adjustment. Also on an unknown date, left cardiac catheterisation was carried out, a new stent was not placed. Post-operatively, the patient experienced Hb-relevant bleeding in the clinic after the red cell concentrates had been administered. The patient then received a further course of four red cell concentrates, whereupon his general condition clearly improved. During his time in hospital, the patient had nose bleeding twice, with another minor bleeding after they injured his lower leg. The patient's thrombocytopenia improved only marginally and his/her leukocytopenia returned to the normal range. The results of a blood smear are still pending and will be submitted at a later date. Since the patient had lost appetite, a gastroscopy carried out which revealed a clear oesophageal thrush. For that reason, the patient's medication was extended to include Ampho-Moronal, in lozenge form, 1-1-1-1 for another six weeks. If the patient's complains don't resolve, the medication was to be adjusted, if necessary, and to request a new gastroscopy check-up. Action taken with the suspect drug was not reported. Outcome of the adverse event was recovered on 12-Oct-2012. On 15-Oct-2012 at 10:26, the patient's hemoglobin was at 8.4 g/dl (normal range: 13.5-17.5), hematocrit was at 26.8 % (normal range: 40-53), CK was at 18 U/L (normal value: less than 190), CK-MB was at 23 U/L (normal value: less than 25), quick was at 91% (normal value: greater than 70), INR (international normalized ratio) was at 1.06 (normal value: less than 1.3; unit not reported), and PTT was at 46 sec (normal value: less than or equal 40). On 18-Oct-2012 at 13:16, the patient's hemoglobin was at 10.0 g/dl, hematocrit was at 29.8 %, quick at 88%, INR at 1.10, PTT at 47 sec., and fibrinogen at 326 mg/dl (normal range: 200-400). On 19-Oct-2012 at 10:41, the patient's hemoglobin was at 9.7 g/dl, hematocrit was at 30.2 %, quick at 86%, INR at 1.10, and PTT at 44 sec. On 22-Oct-2012 at 13:25, the patient's hemoglobin was at 8.7 g/dl, hematocrit was at 25.8 %, quick at 77%, and INR at 1.21. On 24-Oct-2012 at 10:18, the patient's hemoglobin was at 8.8 g/dl, hematocrit was at 27.7 %, quick at 80%, INR at 1.15, and PTT at 41 sec. The patient was discharged from the hospital on 25-Oct-2012. The reporter's causality assessment for the event of NSTEMI in relation to epoetin zeta was not related. Risk factors included coronary heart disease, myocardial infarction, atrial fibrillation, hypertension and history of smoking. 02-Feb-2015: Additional information was received from the investigator regarding patient's age, concomitant medications, dose of Retacrit prior to the adverse event, laboratory tests; description (chest pain), treatment and outcome of the adverse event; and reporter's causality assessment. Hospitalization was added as a seriousness criterion. Ischemic heart disease and peripheral arterial disease were added to patient's medical history. It was also reported that the patient had no previous exposure to other biosimilars. First dose of Retacrit was also reported as 6000 (unit not reported). Onset date of the event was changed to 11-Oct-2012. Date of discharge from the hospital was also provided. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number, date of expiry. 06-Feb-2015: Translation of German narrative was received.
Medical history of thromboendarterectomy, quadruple aortocoronary venous bypass, occlusion of the right cardiac artery, severe stenosis of RIVA and RCX, LIMA on RIVA, mild aortic insufficiency, abdominal aortic aneurysm, pulmonary emphysema with stage II COPD, benign prostatic hyperplasia, vocal cord paresis, post-status abdominal wall haematoma during Arixtra administration, TAA status post atrial thrombus, heparin-induced thrombocytopenia, myelodysplastic syndrome with anaemia, post-status amiodarone induced hypothyroidism, left side ischemic heart disease, peripheral arterial disease with the disobliteration of the left femoral artery in Mar-2012, and post left cardiac catheterization were

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

added. Physical examination and ECG results were also added. It was reported that ASS was discontinued for the time being. Route of administration of Spiriva and Oxis was provided. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Event is possibly related as Retacrit can theoretically increase the risk of thromboembolic events by increasing red cell concentration, but cannot provide a more definitive assessment without further objective
clinical event details. - N. Gonzales (03 Oct 2014) Follow-up: Overall case causality: Not related New information and a more detailed medical history noted. Causality updated to not related as patient had preexistent ischemic heart
disease and arteriosclerosis even prior to start of the suspect drug. Patient still also had low hemoglobin values during the event, making it more unlikely for the drug to have a causative role. - N. Gonzales (10 Feb 2015) Follow-up: No change from last assessment. - N. Gonzales (13 Feb 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	15-OCT-2012	Activated partial thromboplastin time	46 seconds	
2	18-OCT-2012	Activated partial thromboplastin time	47 seconds	
3	19-OCT-2012	Activated partial thromboplastin time	44 seconds	
4	24-OCT-2012	Activated partial thromboplastin time	41 seconds	
5	15-OCT-2012	Blood creatine phosphokinase	18 IU/l	
6	15-OCT-2012	Blood creatine phosphokinase MB	23 IU/l	
7	18-OCT-2012	Blood fibrinogen	326 mg/dl	400 200
8		Breath sounds	No crackles,Unknown	
9		Breath sounds	Vesicular breath sounds bilateral ,Unknown	
10		Electrocardiogram	Maximum RR distance 1.9 sec,Unknown	
11		Electrocardiogram	Minimum 65 beats/min, maximum 114 beats/min,,Unkno	
12		Electrocardiogram	Continuous AA in VHF, HF 73 beats/ min,Unknown	
13		Electrocardiogram	Prolonged RR:Normal in the centre,Unknown	
14		Electrocardiogram	49 polymorphic VES, isolated couplets,Unknown	
15		Electrocardiogram	Low to normal values at night, good RR adjustment,	
16	11-OCT-2012	Electrocardiogram	leads I, II and III, aVF, V4-V6,Unknown	
17	11-OCT-2012	Electrocardiogram	AA at normal heart rate, negative Twave in,Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
18		Gastrointestinal examination	Peristaltic sounds normal ,Unknown	
19		Gastrointestinal examination	Soft, no tenderness,Unknown	
20	15-OCT-2012	Haematocrit	26.8 %	53 40
21	18-OCT-2012	Haematocrit	29.8 %	53 40
22	19-OCT-2012	Haematocrit	30.2 %	53 40
23	22-OCT-2012	Haematocrit	25.8 %	53 40
24	24-OCT-2012	Haematocrit	27.7 %	53 40
25	15-OCT-2012	Haemoglobin	8.4 g/dl	17.5 13.5
26	18-OCT-2012	Haemoglobin	10.0 g/dl	17.5 13.5
27	19-OCT-2012	Haemoglobin	9.7 g/dl	17.5 13.5
28	22-OCT-2012	Haemoglobin	8.7 g/dl	17.5 13.5
29	24-OCT-2012	Haemoglobin	8.8 g/dl	17.5 13.5
30		Heart sounds	Clear and arrhythmic no cardiac murmurs,Unknown	
31	15-OCT-2012	International normalised ratio	1.06,Unknown	
32	18-OCT-2012	International normalised ratio	1.10,Unknown	
33	19-OCT-2012	International normalised ratio	1.10,Unknown	
34	22-OCT-2012	International normalised ratio	1.21,Unknown	
35	24-OCT-2012	International normalised ratio	1.15,Unknown	
36		Neurological examination	No fresh neurological deficits,Unknown	
37		Pain assessment	No throbbing pain in the renal capsule,Unknown	
38		Prothrombin time	86 %	
39		Prothrombin time	88 %	
40		Prothrombin time	80 %	
41		Prothrombin time	91 %	
42		Prothrombin time	77 %	

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCCINATE) ; Unknown

#7) MST /00021210/ (MAGNESIUM SALICYLATE) ; Unknown

#8) OXIS (FORMOTEROL FUMARATE) ; Unknown

#9) PANTOZOL /01263204/ (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Unknown

#10) RANEXA (RANOLAZINE) ; Unknown

#11) SPIRIVA (TIOTROPIUM BROMIDE) ; Unknown

#12) TOREM /01036501/ (TORASEMIDE) ; Unknown

#13) XARELTO (RIVAROXABAN) ; Unknown

#14) XIPAMID (XIPAMIDE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Medical history included thromboendarterectomy of the left internal carotid artery in 1998, quadruple aortocoronary venous bypass (AVCB) carried out in Apr-2003, occlusion of the right cardiac artery (RCA), severe stenosis of RIVA and RCX, LIMA on RIVA, mild aortic insufficiency, abdominal aortic aneurysm (not more than 4 cm in width), pulmonary emphysema with stage II COPD treated with oxygen therapy, benign prostatic hyperplasia, vocal cord paresis (left side), post-status abdominal wall haematoma during Arixtra administration, TAA status post atrial thrombus in July-2009, heparin-induced thrombocytopenia, myelodysplastic syndrome with anaemia treated with 4 red cell concentrate transfusions, post-status amiodarone-induced hypothyroidism, left side ischemic heart disease, peripheral arterial disease with the disobliteration of the left femoral artery in Mar-2012, atrial fibrillation; and arteriosclerosis which led to renal failure diagnosed in Jan-2011. The patient had status post left cardiac catheterisation on 08-Oct-2012. It was reported that the patient was not on dialysis, and had not received Retacrit prior to the study. The patient was not treated with an ESA before treatment with Retacrit. The patient had no previous exposure to other biosimilars. Risk factors included coronary heart disease, myocardial infarction, atrial fibrillation, hypertension and history of smoking. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Benign prostatic hyperplasia (Benign prostatic hyperplasia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Aortic valve insufficiency (Aortic valve incompetence);
Unknown to Ongoing	Relevant Med History	Myelodysplastic syndrome (Myelodysplastic syndrome);
Unknown to Ongoing	Relevant Med History	Oesophageal thrush (Oesophageal candidiasis);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Emphysema pulmonary (Emphysema);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	COPD (Chronic obstructive pulmonary disease);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Vocal cord paresis (Vocal cord paresis);
Unknown	Relevant Med History	Abdominal aortic aneurysm (Aortic aneurysm);
Unknown	Relevant Med History	Atrial thrombosis (Atrial thrombosis);
Unknown	Relevant Med History	Abdominal wall haematoma (Abdominal wall haematoma);
Unknown	Relevant Med History	Femoral artery injury (Arterial injury);
Unknown	Relevant Med History	Heparin-induced thrombocytopenia (Heparin-induced thrombocytopenia);
Unknown	Relevant Med History 8-Oct-2012	Cardiac catheterisation (Catheterisation cardiac);
Unknown	Relevant Med History	Coronary artery occlusion (Coronary artery occlusion);
Unknown	Relevant Med History in April 2003	Aortocoronary bypass (Coronary artery bypass);
Unknown	Relevant Med History	Arterial stenosis (Arterial stenosis);
Unknown	Relevant Med History in 1998	Thromboendarterectomy (Endarterectomy);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Acquired hypothyroidism (Hypothyroidism);
Unknown	Relevant Med History	Cardiac catheterisation (Catheterisation cardiac);
Unknown	Relevant Med History	Oxygen supplementation (Oxygen therapy);
Unknown	Relevant Med History	Blood product transfusion (Transfusion);
Unknown	Past Drug Event	AMIODARONE (AMIODARONE); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Acquired hypothyroidism (Hypothyroidism)
Unknown	Past Drug Event	ARIXTRA (ARIXTRA); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Abdominal wall haematoma (Abdominal wall haematoma)
Unknown	Past Drug Event	HEPARIN (HEPARIN); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction:

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		Heparin-induced thrombocytopenia (Heparin-induced thrombocytopenia)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	24	DEC	1944	69 Years	Female	55.00 kg	03	JUN	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Left leg deep thrombosis [Deep vein thrombosis]
Lung embolism [Pulmonary embolism]

Case Description: Left leg deep thrombosis, lung embolism. Epoetin zeta. Serious Hospira sponsored clinical study report from Germany received from an investigator (reference: Ge-142-0026) which refers to a 69-year-old Caucasian female patient (height:
164 cm, dry weight: 55 kg). The patient was enrolled in a PASCO II: Post Authorisation Safety Cohort Observation of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) Freq: 2 week, Interval

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 20-APR-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOBETA (ALLOPURINOL) Tablet ; Unknown
#2) ASS (ACETYLSALICYLIC ACID) Tablet ; Unknown
#3) CANDESARTAN CILEXETIL (CANDESARTAN CILEXETIL) Tablet ; Unknown
#4) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCC
#5) BICANORM (SODIUM BICARBONATE) Tablet ; Unknown
#6) CERTICAN (EVEROLIMUS) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Depressive episode (Depression)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2595685

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-OCT-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Patient's medical history
included polycystic kidney disease which led to renal failure diagnosed in Dec-2003. The patient was neither pregnant nor lactating. It was reported that the patient was not on dialysis. It was reported that the patient had not been exposed to other erythropoetin-stimulating agent and to other biosimilars. Concomitant medications included Uro-Tablinen tablet (1-0-0-0) for prophylaxis; Allobeta 100 tablet (1-0-0-0) against uric acid; prednisone tablet (5 mg, 1-0-0-0), Certican 0.75 mg tablet (1-0-1-0), Certican 1 mg tablet (0-0-0-0; target level 5), Ezetrol 10 mg tablet (2-0-0-0), Pantozol 40 mg enteric-coated tablet (1-0-0-1), ASS Hexal 100 mg tablet (1-0-0-0, every 2 days), L-thyroxine beta 50 mcg tablet (1-0-0-0), Beloc-Zok 95 mg retard tablet (1-0-1-0), Dekristol capsule (20000 IE, every 14 days), Atacand 16 mg tablet (candesartan cilexetil; 1-0-1-0), Novalgin 500 mg/ml drops (if required, dose not reported), spironolactone 50 mg tablet (1/2-0-0-0), MCP-beta (20 drops, if required), BicaNorm enteric coated tablet (1-0-1-0), Torasemid 10 mg tablet (1/2-0-0-0), alendronate Stada 70 mg tablet (1-0-0-0; break from Mar-2014) given for unknown indications. Routes of administration not reported for all concomitant medications. On 20-Apr-2011, the patient started treatment with epoetin zeta (epoetin zeta, 2x/week, subcutaneous, batch number unknown; dose not reported) for renal anaemia. The patient also had received Retacrit (150 IU/kg/week; route of administration not reported) on 14-Nov-2011. Date of enrollment was on 26-Mar-2013. Current treatment of Retacrit during week of entry on 21-Nov-2012 was administered at a dose of 36 IU/kg/week, 1 dosage/week. On 19-Mar-2014, creatinine was 2.19 (normal range: 0.5-0.9), Hb was 10.3 g/dl (normal range: 12-15.5), haematocrit was 31 % (normal range: 40-51), erythrocyte was 3.80 (normal range: 4.3-5.6), leukocyte was 13.00 (normal range: 4.3-10), thrombocyte was 171 (normal range: 150-400), MCV was 82.0 (normal range: 80-96) and CRP was 4.50 (normal range: less than 5). On 28-Mar-2014, Hb was 11.7 g/dl, haematocrit was 36%, creatinine was 3.13, CRP of 1.90, sO2 was 98.7%, pO2 was 103 mmHg (normal range not reported) and pCO2 was 37.0 mmHg (normal range not reported). On 08-Apr-2014, Hb was 13.6 g/dl, haematocrit was 42%, creatinine was 2.61, Hb was 10.8 g/dl, haematocrit was 33.0 %, erythrocytes was 4.00, leukocytes was 9.40, thrombocytes was 264, MCV was 82.0, CRP was 0.90, sO2 was 97.6%, pO2 was 85 mmHg and pCO2 was 33.2 mmHg. On 03-Jun-2014, the patient experienced left leg deep thrombosis and both lung embolism, described as 4 level thrombosis. It was reported that dyspnoea was the reason of the hospitalisation on 03-Jun-2014. On an unknown date, a scintigraphy was done with suspicion of lung embolism. On an unknown date, a duplex was done and results showed deep thrombosis of leg. Treatment for the adverse events included anticoagulation with heparin initially and later on phenprocoumon therapy (warfarine); doses and routes of administration not reported.
Action taken with the suspect drug in response to the adverse events was not reported. Outcome of the adverse events was recovered on 08-Jul-2014 and the patient was discharged from the hospital. On 15-Sep-2014, creatinine was 2.00, Hb was 11.1 g/dl, haematocrit was 36.0 %, erythrocytes was 3.90, leukocytes was 7.40, thrombocytes was 375, MCV was 92.0 and CRP was 1.60. On 16-Sep-2014, Hb was 14.5 g/dl, haematocrit was 45%, sO2 was 36.8% and pCO2 was 54.0 mmHg. On 02-Oct-2014, Hb was 14.2 g/dl, haematocrit was 44%, creatinine was 2.51, Hb was 11.9 g/dl, haematocrit was 38.0 %, erythrocyte was 4.30, leukocyte was 7.40, thrombocyte was 227, MCV was 89.0, CRP was 0.40, SO2 was 30.5%, and pCO2 was 52.1 mmHg. On 07-Oct-2014, Hb was 13.9 g/dl, haematocrit was 43%, sO2 was 31.6% and pCO2 was 45.9 mmHg. The reporter’s opinion of causality for the events of left leg deep thrombosis and lung embolism in relation to epoetin zeta was not related.Alternative etiologies included immobilization of the patient due to depressive episodes. It was reported that as a transplant recipient, the patient was at a high risk for vessel diseases. Risk factors included peripheral arterial disease, cerebrovascular disease, stroke, hyperlipidaemia, hypertension since Dec-2003, heart failure NYHA III, vascular risk of patient due to long-term immunosupression after transplantation and heart insufficiency since Jun-2007. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dose administered. 27-Oct-2014: Additional information was received from the investigator. Follow-up report was created to reflect that the patient did not have previous exposure to other biosimilar products and to reflect information regarding alternative etiologies that could explain the adverse events. This information has been incorporated in the narrative.

Case Comment: Overall case causality: Probably Not Although the suspect drug can theoretically increase the risk of thrombosis, patient has multiple risk factors for ischemia, which far outweigh the potential risk from the suspect drug. - N. Gonzales (26 Oct 2014) Follow-up: New information noted but does not warrant change in previous causality assessment. Case remains probably not related to the suspect drug based on previously stated rationale. - N. Gonzales (04 Nov 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	19-MAR-2014	Blood creatinine	2.19, Unknown	0.9 0.5
2	28-MAR-2014	Blood creatinine	3.13, Unknown	0.9 0.5
3	08-APR-2014	Blood creatinine	2.61, Unknown	0.9 0.5
4	15-SEP-2014	Blood creatinine	2.00, Unknown	0.9 0.5
5	02-OCT-2014	Blood creatinine	2.51, Unknown	0.9

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ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				0.5
6	19-MAR-2014	C-reactive protein	4.50, Unknown	
7	28-MAR-2014	C-reactive protein	1.90, Unknown	
8	08-APR-2014	C-reactive protein	0.90, Unknown	
9	15-SEP-2014	C-reactive protein	1.60, Unknown	
10	02-OCT-2014	C-reactive protein	0.40, Unknown	
11	19-MAR-2014	Haematocrit	31 %	51 40
12	28-MAR-2014	Haematocrit	36 %	51 40
13	08-APR-2014	Haematocrit	42 %	51 40
14	08-APR-2014	Haematocrit	33.0 %	51 40
15	15-SEP-2014	Haematocrit	36.0 %	51 40
16	16-SEP-2014	Haematocrit	45 %	51 40
17	02-OCT-2014	Haematocrit	44 %	51 40
18	02-OCT-2014	Haematocrit	38.0 %	51 40
19	07-OCT-2014	Haematocrit	43 %	51 40
20	19-MAR-2014	Haemoglobin	10.3 g/dl	15.5 12
21	28-MAR-2014	Haemoglobin	11.7 g/dl	15.5 12
22	08-APR-2014	Haemoglobin	10.8 g/dl	15.5 12
23	08-APR-2014	Haemoglobin	13.6 g/dl	15.5 12
24	15-SEP-2014	Haemoglobin	11.1 g/dl	15.5 12
25	16-SEP-2014	Haemoglobin	14.5 g/dl	15.5 12
26	02-OCT-2014	Haemoglobin	14.2 g/dl	15.5 12
27	02-OCT-2014	Haemoglobin	11.9 g/dl	15.5 12
28	07-OCT-2014	Haemoglobin	13.9 g/dl	15.5 12
29	19-MAR-2014	Mean cell volume	82.0, Unknown	96 80
30	08-APR-2014	Mean cell volume	82.0, Unknown	96 80
31	15-SEP-2014	Mean cell volume	92.0, Unknown	96 80

Mfr. Control Number: 2595685

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
32	02-OCT-2014	Mean cell volume	89.0, Unknown	96 80
33	28-MAR-2014	Oxygen saturation	98.7 %	
34	08-APR-2014	Oxygen saturation	97.6 %	
35	16-SEP-2014	Oxygen saturation	36.8 %	
36	02-OCT-2014	Oxygen saturation	30.5 %	
37	07-OCT-2014	Oxygen saturation	31.6 %	
38	28-MAR-2014	PCO2	37.0 mmHg	
39	08-APR-2014	PCO2	33.2 mmHg	
40	16-SEP-2014	PCO2	54.0 mmHg	
41	02-OCT-2014	PCO2	52.1 mmHg	
42	07-OCT-2014	PCO2	45.9 mmHg	
43	28-MAR-2014	PO2	103 mmHg	
44	08-APR-2014	PO2	85 mmHg	
45	19-MAR-2014	Platelet count	171, Unknown	400 150
46	28-MAR-2014	Platelet count		400 150
47	08-APR-2014	Platelet count	264, Unknown	400 150
48	15-SEP-2014	Platelet count	375, Unknown	400 150
49	02-OCT-2014	Platelet count	277, Unknown	400 150
50		Radioisotope scan	Suspicion of lung embolism, Unknown	
51	19-MAR-2014	Red blood cell count	3.80, Unknown	5.6 4.3
52	08-APR-2014	Red blood cell count	4.00, Unknown	5.6 4.3
53	15-SEP-2014	Red blood cell count	3.90, Unknown	5.6 4.3
54	02-OCT-2014	Red blood cell count	4.30, Unknown	5.6 4.3
55		Ultrasound Doppler	Showed deep thrombosis of leg, Unknown	
56	19-MAR-2014	White blood cell count	13.00, Unknown	10 4.3
57	28-MAR-2014	White blood cell count		10 4.3

Mfr. Control Number: 2595685

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
58	08-APR-2014	White blood cell count	9.40, Unknown	10 4.3
59	15-SEP-2014	White blood cell count	7.40, Unknown	10 4.3
60	02-OCT-2014	White blood cell count	7.40, Unknown	10 4.3

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCCINATE) Tablet ; Unknown

#7) DEKRISTOL (COLECALCIFEROL) Capsule ; Unknown

#8) EZETROL (EZETIMIBE) Tablet ; Unknown

#9) MCP BETA (METOCLOPRAMIDE HYDROCHLORIDE) ; Unknown

#10) NOVALGIN /00169801/ (CAFFEINE, PARACETAMOL, PROPYPHENAZONE) Tablet ; Unknown

#11) PANTOZOL /01263204/ (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

#12) TORASEMID (TORASEMIDE) Tablet ; Unknown

#13) URO-TABLINEN (NITROFURANTOIN) Tablet ; Unknown

#14) ALENDRONATE (ALENDRONATE SODIUM) Tablet ; Unknown

#15) L-THYROXINE /00068001/ (LEVOTHYROXINE) Tablet ; Unknown

#16) PREDNISONE (PREDNISONE) Tablet ; Unknown

#17) SPIRONOLACTONE (SPIRONOLACTONE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption and tobacco usage were not reported. Patient's medical history included polycystic kidney disease which led to renal failure diagnosed in Dec-2003. The patient was neither pregnant nor lactating. It was reported that the patient was not on dialysis. It was reported that the patient had not been exposed to other erythropoetin-stimulating agent and to other biosimilars. Alternative etiologies included immobilization of the patient due to depressive episodes. It was reported that as a transplant recipient, the patient was at a high risk for vessel diseases. Risk factors included peripheral arterial disease, cerebrovascular disease, stroke, hyperlipidaemia, hypertension since Dec-2003, heart failure NYHA III, vascular risk of patient due to long-term immunosupression after transplantation and heart insufficiency since Jun-2007. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Polycystic kidney (Congenital cystic kidney disease);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Transplant tenderness (Complications of transplant surgery);
Unknown	Relevant Med History	Unspecified cerebrovascular disease (Cerebrovascular disorder);

Mfr. Control Number: 2595685

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);
Unknown	Relevant Med History	Heart insufficiency (Cardiac failure);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Immobile (Immobile);
Unknown	Relevant Med History	Immunosuppression (Immunosuppression);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Stroke (Cerebrovascular accident);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	17	DEC	1938	75 Years	Female	78.40 kg	01	OCT	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Chest pain [Chest pain]
Myocardial infarction [Myocardial infarction]
Shortness of breath [Dyspnoea]

Case Description: Myocardial infarction, chest pain, shortness of breath. Epoetin zeta. Serious Hospira-sponsored study report from Sweden, received from an investigator (reference: Sw-018-0012), which refers to a 75-year-old Caucasian female patient
(dry weight: 78.4 kg, height: 158 cm). Medical history included diabetic nephropathy which led to renal failure diagnosed in Feb-2009.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 4000 E, every second week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) haematopoiesis (Bone marrow failure)

18. THERAPY DATES(from/to)
#1) 29-FEB-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALFADIL (DOXAZOSIN MESILATE) Tablet ; Unknown
#2) ALLOPURINOL NORDIC DRUGS (ALLOPURINOL) Tablet ; Unknown
#3) ALVEDON (PARACETAMOL) Tablet ; Unknown
#4) AMLODIPIN ACTAVIS /00972402/ (AMLODIPINE BESILATE) Tablet ; Unknown
#5) FURIX (FUROSEMIDE) Tablet ; Unknown
#6) GLYTRIN (GLYCERYL TRINITRATE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2653063

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-DEC-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The pateint was not on dialysis. The patient was not at any time exposed to any other erythropoietinstimulating agent (ESA) and had no previous exposure to other biosimilars. Concomitant medications included Insulatard FlexPen injection liquid 100 IU/ml suspension in a pre-filled injection pen (20 E in the evening), metoprolol GEA Retard 50 mg prolonged release tablet (0.5 tablet once a day, also reported as 0.5x1), NovoRapid FlexPen injection liquid 100 U/ml solution in a pre-filled injection pen (mealtime insulin, also reported as 10+10+10), and prednisolone Altemova 5 mg tablet (cortisone according to a separate schedule; dose and route of administration not reported) for unknown indications; Alfadil 4 mg prolonged release tablet (1 tablet 2 times daily, also reported as 1x2) for blood pressure, allopurinol 100 mg tablet (1 tablet once a day, also reported as 1x1) for rheumatism, Almodipin Actavis 10 mg tablet (1 tablet daily, also reported as 1x1) for hypertension, Furix 40 mg tablet (3 tablet for breakfast, 2 tablets for lunch, also reported as 3+2+0) as diuretic, Glytrin sublingual spray 0.4 mg/dose (1-2 as needed, sublingually) for vascular spasm or angina pectoris, omeprazole Actavis 20 mg hard gastroresistant capsule (1 tablet once a day, also reported as 1x1) as gastroprotective, Plavix 75 mg film coated tablet (1 tablet once a day, also reported as 1x1) to prevent blood clots, Renvela 800 mg film coated tablet (1 tablet for breakfast and one for dinner, also reported as 1x2) to lower the phosphate value, simvastatin Arrow 20 mg film coated tablet (1 tablet in the evening, also reported as 1x1) for blood lipids, Trombyl 75 mg tablet (1 tablet daily, also reported as 1+0+0+0) for prevention of blood clots, and Alvedon 665 mg tablet with modified release (1-2 tablets, 1-3 times daily, as needed, also reported as 1-2x1-3, Vb) for aches; routes of administration not reported. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. On 29-Feb-2012, the patient started treatment with Retacrit (epoetin zeta, 4000 E every second week, also reported as every other week, subcutaneous, injection liquid solution pre-filled syringe 4000 IU/0.4 ml, lot number unknown) for haematopoiesis. On 14-Jun-2013, the patient was enrolled in the study. During week of entry into study, the patient received Retacrit with total dosage of 50 IU/kg/week, 1 dosage/week. On 01-Oct-2014, the patient experienced myocardial infarction, chest pain, and shortness of breath. The patient was admitted to a hospital because of the adverse events on 05-Oct-2014. On the same day at 15:36, laboratory results showed a heart attack with high troponin-I (TNI) at 2.8 ug/L (normal value: less than 0.070 ug/L); Hb at 111 g/L (normal values: 117-153), CRP at 56 mg/L (normal value: less than 4.0), and creatinine at 256 mcmol/L (normal values: 45-90). Further investigations revealed the following: on 06-Oct-2014 at 07:30, CRP was at 62 mg/L, creatinine at 249 mcmol/L, and troponin-I at 2.8 ug/L and on 09-Oct-2014 at 07:45, CRP was at 40 mg/L and creatinine at 308 mcmol/L. Treatment for the adverse events included Arixtra, Trombyl, and Plavix (doses and routes of administration not reported). Action taken with the suspect drug in reponse to the adverse events was not reported. The patient recovered from the events of myocardial infarction, chest pain, and shortness of breath on 10-Oct-2014. The patient was discharged from the hospital on the same day. On 05-Nov-2014, laboratory test showed Hb at 113 g/L, CRP at 6.2 mg/L, and creatinine at 294 mcmol/L. The reporter's opinion of causality between the events of myocardial infarction, chest pain, and shortness of breath and suspect drug epoetin zeta was not related. Risk factors included stroke and type 2 diabetes with diabetic vascular complications. 05-Dec-2014: Received English translation of the Swedish text. Follow up report created to reflect new information regarding concomitant medications. Formulation of Retacrit was provided and its indication for use was updated to haematopoiesis. This information has been incorporated in the narrative and corresponding data fields. 17-Dec-2014: Additional information received from the same reporter. The reporter was able to provide the following information for the identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. This information has been incorporated in the narrative.

Case Comment: Overall case causality: Possible Events are considered possibly related as suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration. Consider also contributory effects of cardiovascular risk factors in the medical history. - N. Gonzales (03 Dec 2014) Follow-up: New information noted, but does not warrant change in previous causality assessment. - N. Gonzales (12 Dec 2014) Follow-up: No change in previous assessment. Case remains possibly related. - N. Gonzales (23 Dec 2014)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	05-OCT-2014	Blood creatinine	256,MCMOL/L	90 45
2	06-OCT-2014	Blood creatinine	249,MCMOL/L	90 45
3	09-OCT-2014	Blood creatinine	308,MCMOL/L	90 45
4	05-NOV-2014	Blood creatinine	294,MCMOL/L	90 45
5	05-OCT-2014	C-reactive protein	56 mg/l	
6	06-OCT-2014	C-reactive protein	62 mg/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	09-OCT-2014	C-reactive protein	40 mg/l	
8	05-NOV-2014	C-reactive protein	6.2 mg/l	
9	05-OCT-2014	Haemoglobin	111 g/l	153 117
10	05-NOV-2014	Haemoglobin	113 g/l	153 117
11	05-OCT-2014	Troponin I	2.8,MCG/L	
12	06-OCT-2014	Troponin I	2.8,MCG/L	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) INSULATARD /00646002/ (INSULIN HUMAN INJECTION, ISOPHANE) Solution for injection in pre-filled syringe ; Unknown

#8) METOPROLOL GEA (METOPROLOL TARTRATE) Tablet ; Unknown

#9) NOVORAPID (INSULIN ASPART) Solution for injection in pre-filled syringe ; Unknown

#10) OMEPRAZOL ACTAVIS (OMEPRAZOLE) ; Unknown

#11) PLAVIX (CLOPIDOGREL BISULFATE) Tablet ; 15-JAN-2004 / Unknown

#12) RENVELA (SEVELAMER CARBONATE) ; Unknown

#13) SIMVASTATIN ARROW (SIMVASTATIN) Tablet ; Unknown

#14) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; Unknown

#15) PREDNISOLONE (PREDNISOLONE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included diabetic nephropathy which led to renal failure diagnosed in Feb-2009. The pateint was not on dialysis. The patient was not at any time exposed to any other erythropoietin-stimulating agent (ESA) and had no previous exposure to other biosimilars. Risk factors included stroke and type 2 diabetes with diabetic vascular complications. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History Feb-2009	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Rheumatism (Rheumatic disorder);
Unknown to Ongoing	Relevant Med History	Vascular spasm (Vasospasm);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);

Mfr. Control Number: 2653063

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	FINLAND	03	JUN	1948	67 Years	Male	104.00 kg	05	NOV	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Worsening of coronary disease [Coronary artery disease]
Transient ischemic attack [Transient ischaemic attack]
Transient ischemic attack [Transient ischaemic attack]
Worsening of coronary disease [Coronary artery disease]

Case Description: Worsening of coronary disease and transient ischemic attack. Epoetin zeta. Hospira sponsored clinical study report, received from an investigator (reference: Fin-002-0002) which refers to a patient.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 60 IU/kg/w (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-NOV-2013 / 19-NOV-2015	#1) 738 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) APURIN SANDOZ (ALLOPURINOL) ; Unknown
#2) ATORVASTATIN ORION (ATORVASTATIN CALCIUM) ; Unknown
#3) BISOPROLOL RATIOPHARM (BISOPROLOL FUMARATE) ; Unknown
#4) BUCORT (HYDROCORTISONE BUTYRATE) ; Unknown
#5) CALCICHEW-D3 (CALCIUM CARBONATE, COLECALCIFEROL) ; Unknown
#6) DUOCORT (HYDROCORTISONE BUTYRATE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2663539

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-APR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had diabetic nephropathy that led to renal failure on 14-Apr-2003. The patient was on haemodialysis since 28-Aug-2013 (3x a week). The patient was not exposed to other erythropoietin-stimulating agents (ESA) prior to treatment with Retacrit. Relevant medical history included atrial fibrillation, COPD, chronic gastrointestinal disease (bleeding), hyperlipidaemia and diastolic cardiac insufficiency. It was reported that coronary angiography was planned, but appears not to have been done. Concomitant medications included warfarin, insulin, bisoprolol Ratiopharm, atorvastatin Orion, lansoprazole Hexal, lactulose Ratiopharm, NovoRapid flex pen, Protaphane flex pen, Etalpha, Calcichew D3 orange, Marevan, Plavix, Primaspan, Venofer 20mg/ml 5 ml inj. liquid (sic), Nitro, Furesis, Bucort 0.1%, DuoCort, Finasterid Rationpharm, Apurin Sandoz, Panadol Extend, Seretide Evohaler, Spiriva Respimat, Mucovin 0.8 mg/ml, Oftan Dexa-Chlora and Oftagel all given for unknown indications. On 12-Nov-2013, the patient began treatment with Retacrit (epoetin zeta, 60 IU/Kg/week, 1 dosage per week, subcutaneous; lot number unknown) for renal anaemia. On 05-Nov-2014, the patient experienced worsening of coronary disease, described as patient complained of dyspnoea during dialysis and labile angina pectoris. The patient was hospitalized on the same day. It was reported that the patient presented due to a deterioration of dyspnea, no chest pain, the dyspnea was so severe that he was unable to walk more than 10-20 meters at a time, before needing to rest. The need for dialytic removal has been rather little, and according to BCM measurements, no excess fluid should be present. It was reported that the dyspnea may be multietiological, but with these risk factors, major coronary disease was possible. On the same day, ECG, chest XR and cardiac tests were requested. ECG revealed nothing new, Chest XR showed no fluid load, P-TnI was 0.043 and BNP was slightly elevated at 425.5 ng/l (Normal values: 0 - 100) and P-CK MBm (Creatinine Kinase Isoenzyme MB Mass) was normal at 0.9 mcg/dl (Normal values: 0 - 7). These were considered as chronic changes. It was reported that if acute ischemia was indicated, therapy should follow accordingly. In the absence of any swelling (which is incompatible with the clinical picture), moving angiography to an earlier date was advised. It was reported that the patient took Astrupin (dose and route of administration not reported) and began PEF monitoring. If case of no radicals, would consider symptoms primarily as cardiac-related and explain when to do an angiography. On the same day of 05-Nov-2014 at 20:13, laboratory results showed pH of 7.460 (unit not reported; Normal values: 7.350 - 7.450), pCO2 of 5.30 (unit not reported; Normal values: 4.50 - 6.50), p02 of 9.60 (unit not reported; Normal values: 11.30 - 13.30); HCO3 of 28.4 mmol/l (Normal values: 22.0 - 28.0), BE of 4.6 mmol/l (Normal values: -2.5-2.5), HbSO2Sat of 95 % (Normal values: 92 - 96), Na of 137 mmol/l, K of 3.9 mmol/l, lactate of 1.5 (Normal values not reported), and Ca-Ion of 1.08 mmol/l (Normal values: 1.18 - 1.30). On 06-Nov-2014, it was reported that the patient was asymptomatic at rest, although with dyspnea, as well as intermittent chest pain during mild exertion; nitroglycerine (dose and route of administration not reported) and rest/pause helped. PEF result was good at 540 l/min (normal range not reported). A cardiac auscultation revealed no murmurs, creaking from the top left in the initial lung inspirium, otherwise clean. P-TnI was stable at 0.040 (unit of measure and normal value not reported). It was reported that angiography was discussed with cardiologist. On the same day of 06-Nov-2014 at 07:00, laboratory results showed CK-MB of 1.1 mcg/L. On 07-Nov-2014, a coronary arterial photo was taken, revealing a long diffuse stenosis from Part A to the beginning of Part b of the LAD. Circulating wall change, wall change in the LOM branch, as well on the right distally. No intervention required there. Treatment for the adverse event was coronary angioplasty. It was reported that cardiologist decided to go with LAD balloon angioplasty. It was reported that there was no problem with wiring. Following this, they still had to go with a balloon size up to 3mm before they achieved a sufficient passage for metal stents, a 3x32 mm metallic stent was deployed distal most [with a pressure of] up to 18 bar (3.6 mm), as was 3x16 mm metallic stent, from the very base of the main body after the circumflex branch to the base of the LAD [with pressure of] up to 22 bar (3.79 mm). It was reported that a pharmaceutical stent could not be deployed. It was reported that after the intervention, the patient was in good health. On 10-Nov-2014 at 08:00, laboratory results showed hemoglobin of 128 (unit not reported; Normal values: 134 - 167), hematocrit of 0.36 (unit not reported; Normal values: 0.39 - 0.50), CRP of 15 mg/L, creatinine of 617 mcg/L (Normal values: 60 - 100) and INR of 2.1 (unit not reported; Normal values: 2.0 - 3.0). On 17-Nov-2014 at 08:52, laboratory results showed INR of 2.1. On 25-Nov-2014 at 09:06, laboratory results showed INR of 1.8. Action taken with the suspect drug was not reported. Outcome for the adverse event was recovered on 10-Nov-2014 and he was discharged from the hospital on the same day. It was recommended that the patient continue with Primaspan, clopidogrel, and Marevan medication for one month, then discontinuing Clopidogrel, [then] a Marevan-Primaspan combination up to one week, followed by Marevan only. On 27-Sep-2015, the patient experienced transient ischemic attack. It was reported that the patient had weakness of arms and dyspnea. Relevant laboratory data included LDL of 1.9 mmol/l and Hb of 137 g/dl (normal values not reported). The patient recovered from the adverse event on 30-Sep-2015. On 23-Oct-2015, the patient had another episode of transient ischemic heart attack. It was reported that the patient came to emergency room due to angina and dyspnoea. He was disoriented and had weakness of hands. Treatment for the adverse event was administration of low molecular weight heparin (dose and route of administration not reported). Action taken with the suspect drug was not reported. The patient recovered from the adverse event on 28-Oct-2015. From 18-Jan-2016 to 22-Jan-2016, the patient was hospitalized due to worsening of coronary disease. Treatment for the event was not reported. The suspect drug was interrupted. However, therapy end date was on 19-Nov-2015. It was reported that the event was persistent. The reporter's opinion of causality between the events epoetin zeta was not related. The reporter's opinion of causality between the events of worsening coronary disease was not related. It was reported that the patient had an adverse event but were not related to Retacrit. Risk factors included obesity, coronary heart disease, peripheral arterial disease, hyperlipidaemia, hypertension, diabetes type 2, heart failure, protein C or S deficiency, antithrombin III deficiency, prothrombin G20210A mutation, homocysteinemia, trauma, vascular anomalies, aneurysm, immobilization and positive familial history. The patient was also a former smoker. 18-Dec-2014: English translation of Finnish report

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

was received. Follow-up report was created to reflect that patient's medical history included COPD and diastolic cardiac insufficiency; information regarding the adverse event and angioplasty treatment were added; ECG, PEF and X-ray results were added. Lansoprazole Hexal, lactulose Ratiopharm, NovoRapid Flex Pen, Protaphane Flex Pen, Etalpha, Calcichew D3 orange, Marevan, Plavix, Primaspan, Venofer, Retacrit, Nitro, Furesis, Bucort, DuoCort, Finasterid Ratiopharm, Apurin Sandoz, Panadol Extend, Seretide Evohaler, Spiriva Respimat, Mucovin, Oftan Dexa-Chlora and Oftagel were added as concomitant medications; proprietary name of bisoprolol and atorvastin were also updated; dose of bisoprolol was updated. This information has been incorporated in the narrative and in the corresponding data fields.
01-Oct-2015: Additional information was received from the same reporter. Transient ischemic heart attack has been added as an adverse event. Ischemic heart disease and chronic gastrointestinal disease (bleeding) were added as medical history. Relevant laboratory result for the new adverse event has also been added. This information has been incorporated in the narrative and in the corresponding data fields. 02-Nov-2015: Additional information was received from the same reporter. New episode of transient ischemic heart attack was added. Life threatening was added as a seriousness criterion. Cessation date of first episode of transient ischemic heart attack was updated to 30-Sep-2015 (previously reported as 29-Sep-2015). This information has been incorporated in the narrative and in the corresponding data fields. 26-Jan-2016: Additional information was received from the same reporter. Date of birth was updated to 03-Jun-1947 (previously Jun 1947); weight was updated to 104 kg (previously 102 kg).Worsening of coronary disease was added as adverse event. Dialysis was updated to haemodialysis. Protein C or S deficiency, antithrombin III deficiency, prothrombin G20210A mutation, homocysteinemia, trauma, vascular anomalies, aneurysm, immobilization, recent pregnancy, recent surgery, and positive familial history were added as risk factors. It was stated that patient was a former smoker (risk factor). Data entry correction was made to reflect hyperlipidemia as medical history in the narrative and to delete cancer and diarrhoea as medical history. This information has been incorporated in the narrative and corresponding data fields.
27 Apr 2016: Additional information was received from the Investigator. It was reported that the patient had an adverse event but were not related to Retacrit. This information was incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Potentially associated with the increased risk of thromboembolic events for the suspect drug, but consider also (non-drug related) progression of underlying coronary disease. Follow-up: No change in assessment. Follow-up: Overall case causality: Related Causality updated to related in accordance with company's binary causality assessment. Both events remain possibly related as suspect drug is known to increase the risk of thromboembolic events. Follow-up: The newly added adverse event of transient ischemic attack is also possibly related as this is also potentially a thromboembolic event. Follow-up: The added adverse event of worsening coronary artery disease is more likely due to natural progression of the underlying disease. Follow-up: Overall case causality: Not realted Noting reporter causality and patient comorbidities, consider events as more likely associated with the progression/evolution of pre-existing conditions with contributory effect from multiple predisposing risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	05-NOV-2014	Base excess	4.6 mmol/l	2.5 -2.5
2	05-NOV-2014	Blood bicarbonate	28.4 mmol/l	28.0 22.0
3	05-NOV-2014	Blood creatine phosphokinase MB	0.9 MCG/DL	7.0 0.0
4	06-NOV-2014	Blood creatine phosphokinase MB	1.1 MCG/L	7.0 0.0
5	10-NOV-2014	Blood creatinine	617 MCG/L	100 60
6	05-NOV-2014	Blood lactic acid	1.5 mmol/l	
7	05-NOV-2014	Blood potassium	3.9 mmol/l	
8	05-NOV-2014	Blood sodium	137 mmol/l	
9	05-NOV-2014	Brain natriuretic peptide	452.5 NG/L	100 0
10	10-NOV-2014	C-reactive protein	15 mg/l	8 0
11	05-NOV-2014	Calcium ionised	1.08 mmol/l	1.30 1.18
12	07-NOV-2014	Cardiac imaging procedure	Long diffuse stenosis form	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			Part A, Unknown	
13	07-NOV-2014	Cardiac imaging procedure	Circulating wall change, wall change in the LOM, U	
14	07-NOV-2014	Cardiac imaging procedure	Branch, as well as on the right distally, Unknown	
15	07-NOV-2014	Cardiac imaging procedure	To the beginning of Part B of the LAD, Unknown	
16	05-NOV-2014	Chest X-ray	No fluid load, Unknown	
17	05-NOV-2014	Electrocardiogram	Revealed nothing new, Unknown	
18	10-NOV-2014	Haematocrit	0.36, Unknown	0.50 0.39
19		Haemoglobin	137 g/l	
20	10-NOV-2014	Haemoglobin	128, Unknown	167 134
21	06-NOV-2014	Heart sounds	Left in the initial lung inspirium, Unknown	
22	06-NOV-2014	Heart sounds	Otherwise clear, Unknown	
23	06-NOV-2014	Heart sounds	Revealed no murmurs, creaking from the top, Unknow	
24	10-NOV-2014	International normalised ratio	2.1, Unknown	3.0 2.0
25	17-NOV-2014	International normalised ratio	2.1, Unknown	3.0 2.0
26	24-NOV-2014	International normalised ratio	1.8, Unknown	3.0 2.0
27		Low density lipoprotein	1.9 mmol/l	
28	05-NOV-2014	Oxygen saturation	95 %	96 92
29	05-NOV-2014	PCO2	5.30, Unknown	6.50 4.50
30	05-NOV-2014	PO2	9.60, Unknown	13.30 11.30
31	06-NOV-2014	Peak expiratory flow rate	540 l/min, Unknown	
32	05-NOV-2014	Troponin I	0.043, Unknown	
33	06-NOV-2014	Troponin I	0.040, Unknown	
34	05-NOV-2014	pH body fluid	7.460, Unknown	7.450 7.350

13. Relevant Tests

Cardiac auscultation(06Nov2014): Revealed no murmurs, creaking from the top, Unknown
Coronary arterial photo (07Nov2014): Circulating wall change, wall change in the LOM, Unknown

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	60 IU/kg/week, Freq: 1 Week, Interval 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	12-NOV-2013 / 19-NOV-2015; 738 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ETALPHA (ALFACALCIDOL) ; Unknown

#8) FINASTERID RATIOPHARM (FINASTERIDE) ; Unknown

#9) FURESIS (FUROSEMIDE) ; Unknown

#10) LACTULOSE RATIOPHARM (LACTULOSE) ; Unknown

#11) LANSOPRAZOLE HEXAL (LANSOPRAZOLE) ; Unknown

#12) MAREVAN (WARFARIN SODIUM) ; Unknown

#13) MUCOVIN (BROMHEXINE HYDROCHLORIDE) ; Unknown

#14) NOVORAPID (INSULIN ASPART) ; Unknown

#15) OFTAGEL (CARBOMER) ; Unknown

#16) OFTAN DEXA-CHLORA (CHLORAMPHENICOL, DEXAMETHASONE) ; Unknown

#17) PANADOL /00020001/ (PARACETAMOL) ; Unknown

#18) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown

#19) PRIMASPAN (ACETYLSALICYLIC ACID) ; Unknown

#20) PROTAPHANE (INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown

#21) SERETIDE (FLUTICASONE PROPIONATE, SALMETEROL XINAFOATE) ; Unknown

#22) SPIRIVA (TIOTROPIUM BROMIDE) ; Unknown

#23) VENOFER (SACCHARATED IRON OXIDE) ; Unknown

#24) INSULIN (INSULIN) ; Unknown

#25) NITRO /00024401/ (NITROFURANTOIN) ; Unknown

#26) WARFARIN (WARFARIN) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. The patient had diabetic nephropathy that led to renal failure on 14-Apr-2003. The patient was on haemodialysis since 28-Aug-2013 (3x a week). The patient was not exposed to other erythropoietin-stimulating agents (ESA) prior to treatment with Retacrit.Relevant medical history included atrial fibrillation, COPD, chronic gastrointestinal disease (bleeding), hyperlipidaemia and diastolic cardiac insufficiency. It was reported that coronary angiography was planned, but appears not to have been done. Race/Ethnicity: Caucasian

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Cardiac insufficiency (Cardiac failure);
Unknown to Ongoing	Relevant Med History	Gastrointestinal bleeding (Gastrointestinal haemorrhage);
Unknown to Ongoing	Relevant Med History	COPD (Chronic obstructive pulmonary disease);
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Aneurysm (Aneurysm);
Unknown	Relevant Med History	Antithrombin III deficiency (Antithrombin III deficiency);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Heart failure (Cardiac failure);
Unknown	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
Unknown	Relevant Med History	Homocystinaemia (Homocystinaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Mobility decreased (Mobility decreased);
Unknown	Relevant Med History	Obesity (Obesity);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Familial risk factor (Familial risk factor);
Unknown	Relevant Med History	Protein C deficiency (Protein C deficiency);
Unknown	Relevant Med History	Protein S deficiency (Protein S deficiency);
Unknown	Relevant Med History	Prothrombin mutation G20210A (Factor II mutation);
Unknown	Relevant Med History	Pregnancy (Pregnancy);
Unknown	Relevant Med History	Surgery (Surgery);
Unknown	Relevant Med History	Trauma (Injury);
Unknown	Relevant Med History	Vascular anomaly (Vascular malformation);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SWEDEN	30	OCT	1935	79 Years	Male	65.00 kg	30	OCT	2014	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Uremia [Azotaemia]
Pulmonary embolism [Pulmonary embolism]

Case Description: Fatal uremia, pulmonary embolism. Epoetin zeta. Serious Hospira sponsored clinical study report from Sweden received from an investigator (reference: Sw-005-0001), which refers to a 79-year-old male Caucasian patient (dry weight: 65
kg, height: 168 cm).

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 28-DEC-2014
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 139 IU/kg, Freq: 1 week, Interval:1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low Hb (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 03-OCT-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Polycystic kidney (Congenital cystic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2706487

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-FEB-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

It was reported that from 14-Dec-1999 to 02-Oct-2011, the patient was treated with Eprex (epoetin alpha, 126 IU/kg/week; route of administration not reported). It was also reported that the patient did not experience any thrombolic event during treatment with Eprex. The patient was enrolled in a Hospira-sponosored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient's medical history included polycystic kidney which led to renal failure diagnosed on an unknown date in 1977 and spinal stenosis. The patient started hemodialysis on 19-Nov-2001 (3 dialysis per week). The patient had not been treated with previous biosimilar product other than Retacrit. Concomitant medications were not reported. On 03-Oct-2011, the patient started treatment with Retacrit (epoetin zeta, 139 IU/kg/week, 1/dosage/week, subcutaneous, lot number unknown) for low HB. Date informed consent was signed was on 13-Feb-2012. On 24-Oct-2014, also reported as 19-Dec-2014, the patient received the last dose of Retacrit prior to the event of pulmonary embolism. On the same day of 24-Oct-2014, haemoglobin was at 105 g/L (normal range not reported) and at 112 g/L on an unknown date. On 30-Oct-2014, the patient experienced pulmonary embolism. However, it was reported that the patient was hospitalized because of the event on 20-Oct-2014. Treatment for the event of pulmonary embolism included anticoagulants (unspecified). On 03-Dec-2014, the patient was discharged from the hospital. On an unknown date, the patient developed uremia. It was reported that the patient decided to stop dialysis treatment due to uremia. Treatment for the adverse event of uremia was not reported. Actions taken with the suspect drug in response to the adverse events were not reported. Outcome of the event of pulmonary embolism was not recovered at the time of the report. On 28-Dec-2014, the patient died. Cause of death was uremia. It was not reported if an autopsy was performed. The reporter's causality assessment of the event of fatal uremia in relation to epoetin zeta was not related, while for the event of pulmonary embolism was unlikely. Risk factors included back pain since 06-Oct-2014, hypoalbuminemia, hypertension, MGUS, myeloma, prostatic cancer in 2003, and urinary bladder cancer diagnosed in Apr-2010, also reported as in 2011. 02-Feb-2015: Additional information was received from the same reporter regarding the previous exposure of the patient to other biosimilars. Data entry correction was also made to correct the reporter's causality in the narrative. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: lot number and date of expiry. 06-Feb-2015: Additional information was received from the same reporter. The adverse event of thromboembolic events was changed to pulmonary embolism. Hospitalization and life threatening were added as seriousness criteria. Additional information was also received regarding the patient's age, update of date of birth, update of weight from 72 kg to 65 kg; date of last dose of Retacrit prior to the adverse event, dose of Eprex; details of the new event: start date, treatment, outcome of the adverse event, and reporter's opinion of causality. Spinal stenosis was added as medical history. It was also reported that the patient did not experience any thrombolic event during treatment with Eprex. Back pain, hypoalbuminemia and MGUS were added as risk factors. Type of dialysis was specified. Indication of Retacrit was changed to low HB. Haemoglobin was added as a laboratory test. Date of admission and discharge from the hospital were also provided. This information has been incorporated in the narrative and in the corresponding data fields

Case Comment: Overall case causality: Possible Fatal uremia is probably not related. Consider the event a likely sequela of the patient's underlying renal disorder. Thromboembolic events is possible. Labeled event, but cannot give a more definitive assessment without further objective clinical event details and a firm timeline. Consider also reported risk factors. - R. Jacot (20 Jan 2015) Follow-up: New information noted. Causality also updated in accordance with the company's new binary causality assessment. Fatal uremia is not related as this is a likely sequela of the patient's underlying chronic renal failure. The thromboembolic event cannot be assessed without further objective clinical event details. - N. Gonzales (09 Feb 2015) Follow-up: Overall case causality: Related New information noted. Causality for pulmonary embolism was updated to related. Suspect drug can theoretically increase the risk of thrombosis by mechanism of action. The increase in hemoglobin was also likely due to the drug. - N. Gonzales (13 Feb 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	112 g/l	
2	24-OCT-2014	Haemoglobin	105 g/l	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption. It was reported that from 14-Dec-1999 to 02-Oct-2011, the patient was treated with Eprex (epoetin alpha, 126 IU/kg/week; route of administration not reported). It was also reported that the patient did not experience any thrombolic event during treatment with Eprex. Patient's medical history included polycystic kidney which led to renal failure

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		diagnosed on an unknown date in 1977 and spinal stenosis. The patient started hemodialysis on 19-Nov-2001 (3 dialysis per week). The patient had not been treated with previous biosimilar product other than Retacrit. Risk factors included back pain since 06-Oct-2014, hypoalbuminemia, hypertension, MGUS, myeloma, prostatic cancer in 2003, and urinary bladder cancer diagnosed in Apr-2010, also reported as in 2011. Race/Ethnicity: Caucasian. On 28-Dec-2014, the patient died. Cause of death was uremia. It was not reported if an autopsy was performed
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Spinal stenosis NOS (Spinal stenosis);
Unknown	Relevant Med History Risk Factor: 06-Oct-2014	Back pain (Back pain);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Hypoalbuminemia (Hypoalbuminaemia);
Unknown	Relevant Med History	MGUS (Hypergammaglobulinaemia benign monoclonal);
Unknown	Relevant Med History	Myeloma (Plasma cell myeloma);
Unknown	Relevant Med History Risk Factor: 2003	Prostate cancer (Prostate cancer);
Unknown	Relevant Med History Risk Factor: 2000	Urinary bladder carcinoma (Bladder cancer);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
14-DEC-1999 to 02-OCT-2011	Past Drug Event	EPOETIN ALFA (EPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	02	JUN	1929	85 Years	Female	64.00 kg	12	NOV	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Transitonic ischaemic event (TIA) [Transient ischaemic attack]

Case Description: Transitonic ischaemic event (TIA). Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (reference: Ge-115-0092), which refers to an 85-year-old female Caucasian patient (dry weight: 64 kg,
height: 154 cm). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 32 IU/kg, Freq: 1 week, Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 25-NOV-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Analgesic nephropathy (Nephropathy toxic)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2721395

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
13-FEB-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

included analgesic nephropathy which led to renal failure diagnosed on Dec-2008. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit and had not received Retacrit prior to the study. Concomitant medications were not reported. The patient's Troponin T on 21-Oct-2010 was negative, less than 0.05 ng/ml (normal range not reported). The patient began treatment with Retacrit (epoetin zeta; 32 IU/kg/week, 1 dosage/week, subcutaneous; lot number unknown) on 25-Nov-2013 for renal anaemia. The patient received last dose of Retacrit at 2000 (unit not reported) prior to the adverse event. On 29-Aug-2014, laboratory tests included Leuko of 5.62/nl (normal range: 3.6 to 9.6), Ery of 4.18/pl (normal range: 3.9 to 5.4), Hb of 12.3 g/dl (normal range: 12.0 to 16.0), Hct of 37.6 % (normal range: 36.0 to 47.0), thrombocytes/PLT of 223/nl (normal range: 150.0 to 400.0), LIP of 35 U/l (normal range: 13.0 to 16.0), Triglycerides (photom) of 271 mg/dl (normal range: less than 200.0), CHOL of 351.7 mg/dl (normal range: less than 200.0), LDL of 203.2 mg/dl (normal range: less than 160.0), HDL of 54.3 mg/dl (normal range: greater than 45.0), and LDL/HDL quotient of 3.7 kA (normal range: less than 3 target value (recomm. Lipid-liga) 3 to 5: inc. risk, greater than 5: high risk). On 12-Nov-2014, the patient experienced acute dysarthria and was admitted to hospital for stroke. On the same day, the patient developed transitonic ischaemic event (TIA). Treatment for the adverse event included heparin (intravenous, dose not reported). Retacrit was not changed and was ongoing in hospital at the time of the report. The patient fully recovered in 24h with event stop date of 12-Nov-2014. The patient was discharged on an unknown day in Nov-2014. On 15-Jan-2015, laboratory tests included Leuko of 7.64/nl, Ery of 4.18/pl, Hb of 12.4 g/dl, Hct of 38.1 %, thrombocytes/PLT of 237/nl, LIP of 34 U/l, Triglycerides (photom) of 216.4 mg/dl, CHOL of 236.4 mg/dl, LDL of 119.7 mg/dl, HDL of 54.3 mg/dl, and LDL/HDL quotient of 2.2 kA. The reporter's opinion of causality between the event of transitonic ischaemic event (TIA) and suspect drug epoetin zeta was unlikely. Risk factor included hypertension. 22-Jan-2015: Additional information was received from the investigator. Adverse event thromboembolic events was changed to transitonic ischaemic event. Seriousness criterion was changed to hospitalization. Additional information was also received regarding patient's age, update of date of birth, update of weight from 62 kg to 64 kg; last dose of Retacrit prior to the adverse event; details of the new event, event start and stop dates, treatment for and outcome of the adverse event, action taken with suspect drug, and reporter's opinion of causality. Date of admission and discharge from the hospital were also provided. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous exposure of patient to other biosimilars. 13-Feb-2015: Corrected report created to reflect that the previously reported additional information was received on 22-Jan-2015 (instead of 03-Feb-2015). This information has been reflected in the narrative and in the corresponding data field. 13-Feb-2015: English translation of the hospital records was received. Laboratory test results were provided. This information has been reflected in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible (reporter causality not assessable) Hospira causality: Not assessable Although the suspect drug can theoretically increase the risk of thrombosis, cannot provide causation of the event without firm timeline of occurrence of the event. Consider also possible contributory effects from unreported risk factors in the medical history. - N. Gonzales (30 Jan 2015) Follow-up: Overall case causality: Related New information regarding timeline noted. Company causality updated to related based on temporal relationship and medical plausibility. Although patient was noted to have a risk factor (hypertension), patient had been using the suspect drug for a year, and this can theoretically increase the risk of thromboembolic events such as TIA. - N. Gonzales (11 Feb 2015) Corrected report: No change in previous assessment. - N. Gonzales (16 Feb 2015) Follow-up: No change in previous assessment. - N. Gonzales (20 Feb 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	29-AUG-2014	Blood cholesterol	351.7 mg/dl	
2	15-JAN-2015	Blood cholesterol	236.4 mg/dl	
3	29-AUG-2014	Blood triglycerides	271 mg/dl	
4	15-JAN-2015	Blood triglycerides	216.4 mg/dl	
5	29-AUG-2014	Haematocrit	37.6 %	47.0 36.0
6	15-JAN-2015	Haematocrit	38.1 %	47.0 36.0
7	29-AUG-2014	Haemoglobin	12.3 mg/dl	16.0 12.0
8	15-JAN-2015	Haemoglobin	12.4 mg/dl	16.0 12.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
9	29-AUG-2014	High density lipoprotein	54.3 mg/dl	
10	15-JAN-2015	High density lipoprotein	54.3 mg/dl	
11	29-AUG-2014	LDL/HDL ratio	3.7 kA, Unknown	
12	15-JAN-2015	LDL/HDL ratio	2.2 kA, Unknown	
13	29-AUG-2014	Lipase	35 IU/l	60.0 13.0
14	15-JAN-2015	Lipase	34 IU/l	60.0 13.0
15	29-AUG-2014	Low density lipoprotein	203.2 mg/dl	
16	15-JAN-2015	Low density lipoprotein	119.7 mg/dl	
17	29-AUG-2014	Platelet count	223/nl, Unknown	400.0 150.0
18	15-JAN-2015	Platelet count	237/nl, Unknown	400.0 150.0
19	29-AUG-2014	Red blood cell count	4.18/pl, Unknown	5.4 3.9
20	15-JAN-2015	Red blood cell count	4.18/pl, Unknown	5.4 3.9
21	21-OCT-2010	Troponin T	Negative, less than 0.5 ng/ml	
22	29-AUG-2014	White blood cell count	5.62/nl Unknown	9.6 3.6
23	15-JAN-2015	White blood cell count	7.64/nl, Unknown	9.6 3.6

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();
		Medical history included analgesic nephropathy which led to renal failure diagnosed on Dec-2008. The patient was not on dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit and had not received Retacrit prior to the study. Allergies, alcohol cosumption and tobacco usage were not reported. Risk factor included hypertension. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History Dec-2008	Renal failure (Renal failure);
Unknown	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	07	JAN	1939	75 Years	Female	78.50 kg	09	DEC	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI(non-ST elevation myocardial infarction) [Acute myocardial infarction]

Case Description: NSTEMI (Non-ST elevation myocardial infarction). Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (ref: Ge-432-0001), which refers to a 75-year-old Caucasian female patient (weight:
78.5 kg; height: 153 cm).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 13 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 30-MAY-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS RATIOPHARM (ACETYLSALICYLIC ACID) Tablet ; Unknown
#2) CALCIUM-DURA (CALCIUM CARBONATE) Tablet ; Unknown
#3) ENAHEXAL /00574902/ (ENALAPRIL MALEATE) Tablet ; Unknown
#4) FERINJECT (FERRIC CARBOXYMALTOSE) ; 29-DEC-2014 / Unknown
#5) INNOLET (INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown
#6) INSULIN ACTRAPID (INSULIN PORCINE) Tablet ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Aortic valve stenosis (Aortic valve stenosis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2735896

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-FEB-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia.
Medical history included s/p PTCA PDA of the RCA in Feb-2006, diabetic nephropathy that led to renal failure diagnosed on 19-Oct-2009, hypertrophied left ventricle, slight aortic valve stenosis, slight mitral valve insufficiency associated with distinct mitral ring calcification, and secondary normocytic normochromic anaemia. The patient was not on dialysis. The patient had no known drug hypersensitivity and no history of drug dependence. Prior to treatment with Retacrit, the patient was treated with Aranesp (darbepoietin, 270 ng/kg/week, subcutaneous; dose also reported as 40 mcg every fortnight to every 4 weeks) from 06-Nov-2009 until 30-May-2012. Concomitant medications included Venofer (1 amp, every distinct mitral ring calcification, and secondary normocytic normochromic anaemia. The patient was not on dialysis. The patient had no known drug hypersensitivity and no history of drug dependence. Prior to treatment with Retacrit, the patient was treated with Aranesp (darbepoietin, 270 ng/kg/week, subcutaneous; dose also reported as 40 mcg every fortnight to every 4 weeks) from 06-Nov-2009 until 30-May-2012. Concomitant medications included Venofer (1 amp, every 12 weeks; route of administration not reported) and Ferinject (500 mg, intravenous infusion, every 4 weeks) both given as iron substitution; carvedilol tablet (12.5 mg, 1-0-1), Enahexal 20/12.5 tablet (0-1-0; dose not reported), amlodipine tablet (5 mg, 1-0-1), Simbaveta tablet (30 mg, 0-0-1), ASS ratiopharm tablet (100 mg, 0-1-0), clopidogrel tablet (75 mg, 0-0-1), Calcium-dura tablet (600 mg/400 IE, 1-0-0, paused), Laxans granulate (paused; dose not reported), pantoprazol tablet (40 mg1-0-0; until 15-Jan-2015: 1-0-1), Targin tablet (5/2.5 mg, 1-0-1; stopped), insulin Actrapid penfill (12-8-8 U; with dose adjustment corrective scheme: blood sugar > 180 mg/dl plus 2 U, blood sugar > 240 mg/dl plus 4 U), Innolet (insulin protaphane, 0-0-0-16 U) (routes of administration not reported); all given for unknown indications. On 30-May-2012, the patient began treatment with Retacrit 1000 U (epoetin zeta, 13 IU/kg/week, frequency also reported as twice weekly Tue plus Fri, subcutaneous, lot number unknown) for renal anaemia. The patient was enrolled in the study on 18-Feb-2013. On 25-Mar-2013, the patient received Retacrit with daily dose reported as 286 E, once weekly. It was reported that the patient had no reaction after receiving the suspect drug. On 09-Dec-2014, the patient experienced NSTEMI (non-ST elevation myocardial infarction). On the same day, the patient came to the hospital with cardiac pain and was treated with conservative therapy (unspecified). The patient presented to her GP due to nausea, loss of appetite, and elevated TnT values. On the same day of 09-Dec-2014, ECG showed heart axis < -30 degrees, SR, HR 76/min, LBBB, and no significant repolarization disturbances. On the same day, RAD thorax (lungs) 2 planes (while standing) showed diaphragmatic elevation due to obesity, heart broadened on both sides, aortic configuration, no cardiac congestion, no pulmonary infiltrate or effusion, sternum cerclage from status post ACB, mitral ring calcification, and osteochondrosis and spondylosisi of the thoracic spine. The patient had a known stage IV renal insufficiency and status post ACB surgery in Jun-2013.
Currently the patient reported exertion dyspnea and loss of appetite. For the past 8 days, the patient had suffered from a cold which involved nausea and chest pressure during exertion. Patient was symptom-free at emergency admission. The GP noted elevated troponin T. The patient was admitted to the Immediate Care Unit on the basis of prior illness and the elevated troponin T value associated with known renal insufficiency. Over time, the patient appeared asymptomatic and troponin T decreased; however, on 10-Dec-2014, a follow-up ECG indicated a negative T in V5/6 (also, heart axis < -30 degrees, SR, and HR 72/min; normal ranges not reported). On the same date at 19:30, laboratory tests done showed the following results: haemoglobin at 9.9 g/dl (normal range: 11.6-16.2), haematocrit at 30.3% (normal range: 35.0-47.0), C-reactive protein at 11.10 mg/l (normal range: 0.0-5.0), CPK at 100 U/l (normal range: 0-145), troponin T at 0.058 ng/ml (normal range: 0.0-0.01), NT-proBNP at 1882 pg/ml (normal value: -624), CK-MB at 15.0 U/l (normal value: -25) and creatinine was at 1.8 mg/dl (normal range: 0.5-0.9). Another follow-up was decided against due to the existing renal insufficiency and the fact that the symptoms were no longer present. On 11-Dec-2014, the patient was transferred with no symptoms to the general care ward. On the same day, high-grade aortic stenosis was excluded on the basis of an echocardiograph (which also showed hypertensive cardiac disease). On the same date at 14:42h, laboratory tests done showed the following results: haemoglobin at 9.1 g/dl, haematocrit at 28.4%, C-reactive protein at 8.52 mg/l, CPK at 121 U/l and creatinine at 1.8 mg/dl. Due to the initial nausea and loss of appetite associated with known anaemia, on 12-Dec-2014, an endo esophagogastroduodenoscopy was arranged which showed erosive pangastritis strongest in the antral region and erosive bulbitis; histology was normal, no hiatus hernia, and HP test antrum/corpus negative. On the same day, int. abdominal sonograph showed liver homogenous, status post CCE, DHC not dilated, right kidney somewhat shrunken, left kidney normal, spleen not enlarged, pancreas normal as far as could be determined, urinary bladder full, no free liquid, no thickening of the intestinal wall. The stomach biopsy samples from the antrum and corpus showed showed slight chronic antral gastritis with stromal fibroses, foveolar hyperplasia with signs of epithelial regeneration, lymphonodular hyperplasia and smooth muscle hyperplasia, no signs of inflammation, histology results indicate helicobacter pylori negative, and no evidence of malignancy; while biopsy samples from stomach corpus with slight focal stromal fibroses and foveolar hyperplasia, no signs of inflammation, no glandular atrophy, histology results indicate helicobacter pylori negative, and no evidence of malignancy. The patient was also diagnosed with BSR increase (80 mm/h). On 15-Dec-2014 at 15:15h, laboratory tests done showed the following results: haemoglobin at 8.1 g/dl, haematocrit at 25.4%, Creactive protein at 4.53 mg/l, CPK at 72 U/l and creatinine at 2.2 mg/dl. On an unknown date, with an Hb decrease from 10 g/dl to 8, the patient was transfused 1 erythrocyte concentrate and increase in Hb to >9. On 17-Dec-2014 at 10:09h, laboratory tests done showed the following results: haemoglobin at 9.1 g/dl, haematocrit at 27.2% and creatinine at 2.5 mg/dl. On 18-Dec-2014, the patient was discharged in stable overall condition and without symptoms. On an unknown date, the patient experienced nausea in the morning with cold sweat, collapsed with loss of consciousness, and contusions II frontal. The patient had no dyspnea, no AP, no cardiac palpitations/irregularities, no bleeding stigmata, currently in ECG SR, negative T-segment shift III, and AV fistula not pre-determined. The patient reported that she first became nauseous then had stomach pain. The patient then suffered syncopes. On 23-Dec-2014, the patient was admitted to the

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

intensive care ward for monitoring of respiration, cardiac function and circulation without measuring pressure of the pulmonary artery or central venous pressure. No significant cardiac arrhythmias were observed during monitoring. On the same date, laboratory tests done showed the following results: haemoglobin at 12:22H was 8.2 g/dl and at 16:06H was 8.2 g/dl, haematocrit at 12:22H was 26.7% and at 16:06H was 24.7%, quick ACL PRO at 12:22H was 110% (normal range: 70-130), INR at 12:22H was 0.98 (normal range: 1.0-1.24), aPTT ACL PRO at 12:22H was 24 sec (normal range: 22-33), C-reactive protein at 12:22H was 4.39 mg/l and at 16:06H was 4.92, CPK at 12:22H was 158 U/l and at 16:06H was 116 U/l, troponin T at 12:22H was 0.042 ng/ml and at 16:06H was 0.037 and creatinine was at 2.9 mg/dl at 12:22h and at 2.5 mg/dl at 16:06. On the same day, RAD thorax (lungs) 2 planes done while standing showed heart was at normal size with no central or peripheral pulmonary congestion, no infiltrate, sternum cerclage. ECG done on the same day showed SR, HR at 59/min, left axis deviation, LSB (QRS 110 ms, negative T in II, AVR, AVF, and V6. The patient requested quick discharge and declined further care as an inpatient at the hospital. There was no further clarification for the syncopation event (long term ECG and echo). On 24-Dec-2014, the patient was discharged in good overall condition. However, laboratory chemistry showed Hb decrease from 9.1 to 8.2 g/dl at discharge (no infusion administered). In response to the event, the dose of Retacrit was increased to 577 U on 29-Dec-2014; frequency from once weekly to twice weekly to 4 times weekly (Mon, Wed, Fri, Sun). It was reported that the event partially improved. Slowly, the patient experienced less pain with higher hemoglobin. On 16-Jan-2015, the patient was admitted for a cardiac catheter examination. The patient reported limited ability to perform activities, experiencing exertional dyspnea even with slight exertion (NYHA III); in addition, the patient described thoracic pressure radiating into the neck, nocturia twice nightly, no edema, and currently no infection causing fever. On an unknown date, physical examination showed no cyanosis, signs of anaemia, icterus; head/neck and thyroid were normal; HT was 2/6 systolic murmur, lungs were clear on both sides, no peripheral edema, normal pulse status, normally oriented neuro status, and no other abnormalities. ECG done on unknown date showed sinus rhythm, heart rate at 71/min, left axis deviation, and complete LBBB with consecutive repolarisation disturbance. On an unknown date, laboratory tests done showed the following results: heamoglobin at 9.5 g/dl, haematocrit at 29%, C-reactive protein at 3.69 mg/l, and CPK at 315 U/l. The cardiac catheter findings indicated a severe 3-vessel coronary artery disease not suitable for intervention. The ACVB to RCA and the LIMA to LAD and T-graft to R.marg (no clinical evidence for A. spurium or AV fistula). On 17-Jan-2015, the patient was transferred to the emergency department from the university hospital with severe 3 vessel coronary artery disease with good overall left ventricular pumping function. On an unknown date, laboratory analyses indicated the known renal insufficiency (creatinine at 1.9). On 19-Jan-2015, INN route ECG showed SR, LT HR at 69/min, RBBB, and no repolarisation disturbances. Findings of physical examination done on an unknown date showed good overall condition and nutritional status, cor: hearttones pure, regular, pulmo: clear, bilateral vesicular breath sounds, no crepitations, abdomen, neurology normal, and no leg edema. In addition, the LT ECG showed no relevant arrhythmias. On an unknown date, haemoglobin was at 9.5 g/dl, haematocrit was at 29%, c reactive protein was at 3.69 mg/l, CPK was at 315 U/l and creatinine was at 1.9 mg/dl. The suspect drug was still ongoing at the time of the report. The patient recovered with sequelae and was discharged on 21-Jan-2015. It was reported that the reaction did not reappear after reintroduction of the suspect drug on an unknown date. The reporter's opinion of causality between the event of NSTEMI (non-ST elevation myocardial infarction) and the suspect drug Retacrit was not related. Risk factors included coronary heart disease, hyperlipidaemia, hypertension, diabetes type 2 with diabetic vascular complications, and obesity. 25-Feb-2015: Additional information was received from the same reporter. Strength of Retacrit was provided. Frequency was also reported as twice weekly Tue plus fri. Medical history were made to include the patient’s diagnoses (erosive pangastritis strongest in the antral region, erosive bulbitis, unexplained BSR increase (80 mm/h) severe 3-vessel coronary artery disease with good overall left ventricular pumping function, s/p PTCA PDA of the RCA in Feb-2006, s/p ACB surgery in Jun-2013, hypertrophied left ventricle, slight aortic valve stenosis, slight mitral valve insufficiency associated with distinct mitral ring calcification, and secondary normocytic normochromic anaemia) and concomitant conditions. Details regarding the patient’s hospitalization were provided. Laboratory tests (haemoglobin, haematocrit, quick ACL PRO, INR, aPTT ACL PRO, C reactive protein, CPK, troponin T and creatinine, biopsy) and diagnostic procedures (ECG, RAD thorax, catheter examination, esophagogastroduodenoscopy, abdominal sonograph) were added. Obesity was added as a risk factor. It was reported that the dose of Retacrit was increased in response to the event. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Not related Although the suspect drug can theoretically increase the risk of thromboembolic events, patient has numerous cardiovascular risk factors, including a preexistent coronary artery disease, which far outweigh the potential risks from the suspect drug. - N. Gonzales (24 Feb 2015) Follow-up: No change in previous causality assessment. - N. Gonzales (05 Mar 2015)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	23-DEC-2014	Activated partial thromboplastin time	24 seconds	33 22
2		Angiocardiogram	Not reported, Unknown	
3		Blood creatine phosphokinase	315 IU/l	145 0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
4	10-DEC-2014	Blood creatine phosphokinase	121 IU/l	145 0
5	11-DEC-2014	Blood creatine phosphokinase	72 IU/l	145 0
6	15-DEC-2014	Blood creatine phosphokinase	158 IU/l	145 0
7	23-DEC-2014	Blood creatine phosphokinase	116 IU/l	145 0
8	23-DEC-2014	Blood creatine phosphokinase	100 IU/l	145 0
9	10-DEC-2014	Blood creatine phosphokinase MB	15.0 IU/l	
10		Blood creatinine	1.9 mg/dl	0.9 0.5
11	10-DEC-2014	Blood creatinine	1.8 mg/dl	0.9 0.5
12	11-DEC-2014	Blood creatinine	1.8 mg/dl	0.9 0.5
13	15-DEC-2014	Blood creatinine	2.2 mg/dl	0.9 0.5
14	17-DEC-2014	Blood creatinine	2.5 mg/dl	0.9 0.5
15	23-DEC-2014	Blood creatinine	2.9 mg/dl	0.9 0.5
16	23-DEC-2014	Blood creatinine	2.5 mg/dl	0.9 0.5
17		Blood pressure measurement	150/70 mmHg	
18		C-reactive protein	3.69 mg/l	5.0 0.0
19	10-DEC-2014	C-reactive protein	11.10 mg/l	5.0 0.0
20	11-DEC-2014	C-reactive protein	8.52 mg/l	5.0 0.0
21	15-DEC-2014	C-reactive protein	4.53 mg/l	5.0 0.0
22	23-DEC-2014	C-reactive protein	4.92 mg/l	5.0 0.0
23	23-DEC-2014	C-reactive protein	4.39 mg/l	5.0 0.0
24		Catheterisation cardiac	for A. spurium or AV fistula), Unknown	
25		Catheterisation cardiac	and T-graft to R.marg. (no clinicalevidence, Unkno	
26		Catheterisation cardiac	A severe 3-vessel coronary artery disease, Unknown	
27		Catheterisation cardiac	not suitable for intervention., Unknown	
28		Catheterisation cardiac	The ACVB to RCA and the LIMA toLAD, Unknown	
29	09-DEC-2014	Chest X-ray	Sternum cerclage from status postACB.Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
30	09-DEC-2014	Chest X-ray	No pulmonary infiltrate or effusion. Unknown	
31	09-DEC-2014	Chest X-ray	Heart broadened on both sides, Unknown	
32	09-DEC-2014	Chest X-ray	Diaphragmatic elevation due toobesity.Unknown	
33	09-DEC-2014	Chest X-ray	and spondylosis of the thoracic spine,. Unknown	
34	09-DEC-2014	Chest X-ray	Mitral ring calcification.Osteochondrosis, Unknown	
35	09-DEC-2014	Chest X-ray	aortic configuration. No cardiaccongestion. Unknow	
36	23-DEC-2014	Chest X-ray	Heart normal size with no central or Unknown	
37	23-DEC-2014	Chest X-ray	peripheral pulmonary congestion, Unknown	
38	23-DEC-2014	Chest X-ray	no infiltrate, sternum cerclage,. Unknown	
39	11-DEC-2014	Echocardiogram	Hypertensive cardiac disease, Unknown	
40		Electrocardiogram	Sinus rhythm,heart rate 71/min, Unknown	
41		Electrocardiogram	left axis deviation,complete LBBB, Unknown	
42		Electrocardiogram	with consecutive repolarisationdisturbance, Unknow	
43	09-DEC-2014	Electrocardiogram	no significant repolarisationdisturbances, Unknown	
44	09-DEC-2014	Electrocardiogram	Heart axis < -30 degrees,SR,HR 76/min,LBBB, Unknow	
45	10-DEC-2014	Electrocardiogram	Heart axis < -30 degrees,SR,HR 72/min,Unknown	
46	10-DEC-2014	Electrocardiogram	T neg V5 + V6 Unknown	
47	23-DEC-2014	Electrocardiogram	SR,HR 59/min,left axis deviation, Unknown	
48	23-DEC-2014	Electrocardiogram	LSB (QRS 110ms),negative T inII,AVR,AVF,V6,Unknown	
49	19-JAN-2015	Electrocardiogram	SR,LT HR 69/min,RBBB,, Unknown	
50	19-JAN-2015	Electrocardiogram	no repolarisation disturbances, Unknown	
51		Haematocrit	29 %	47.0 35.0
52		Haematocrit	29.0 %	47.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				35.0
53	10-DEC-2014	Haematocrit	30.3 %	47.0 35.0
54	11-DEC-2014	Haematocrit	28.4 %	47.0 35.0
55	15-DEC-2014	Haematocrit	25.4 %	47.0 35.0
56	17-DEC-2014	Haematocrit	27.2 %	47.0 35.0
57	23-DEC-2014	Haematocrit	24.7 %	47.0 35.0
58	23-DEC-2014	Haematocrit	26.7 %	47.0 35.0
59		Haemoglobin	9.5 g/dl	16.2 11.6
60	10-DEC-2014	Haemoglobin	9.9 g/dl	16.2 11.6
61	11-DEC-2014	Haemoglobin	9.1 g/dl	16.2 11.6
62	15-DEC-2014	Haemoglobin	8.1 g/dl	16.2 11.6
63	17-DEC-2014	Haemoglobin	9.1 g/dl	16.2 11.6
64	23-DEC-2014	Haemoglobin	8.2 g/dl	16.2 11.6
65	23-DEC-2014	Haemoglobin	8.8 g/dl	16.2 11.6
66	12-DEC-2014	Histology	pylori negative.No evidence ofmalignancy.Unknown	
67	12-DEC-2014	Histology	focal stromal fibroses and foveolarhyperplasia.Unk	
68	12-DEC-2014	Histology	No signs of inflammation.,Histology	
69	12-DEC-2014	Histology	No signs of inflammation.No glandular atrophy.Unkn	
70	12-DEC-2014	Histology	Histology results indicate helicobacter Unknown	
71	12-DEC-2014	Histology	Biopsy samples from stomach corpuswith slight,Unkn	
72	12-DEC-2014	Histology	Slight chronic antral gastritis withstromal,Unknow	
73	12-DEC-2014	Histology	indicate helicobacter pylori negative.Unknown	
74	12-DEC-2014	Histology	hyperplasia and smooth musclehyperplasia.Unkno wn	
75	12-DEC-2014	Histology	No evidence of malignancy. ,Unknown	
76	12-DEC-2014	Histology	fibroses,foveolar hyperplasia withsigns of,	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			Unknow	
77	12-DEC-2014	Histology	epithelial regeneration,lymphonodular, Unknown	
78	23-DEC-2014	International normalised ratio	0.98, Unknown	1.24 1.0
79	10-DEC-2014	N-terminal prohormone brain natriuretic peptide	1882, PG/ML	
80	12-DEC-2014	Oesophagogastroduodenoscopy	Erosive pangastritis strongest in theantral, Unkno	
81	12-DEC-2014	Oesophagogastroduodenoscopy	region and erosive bulbitis.No hiatushernia.Unknow	
82	12-DEC-2014	Oesophagogastroduodenoscopy	HP test antrum/corpus negative Unknown	
83		Physical examination	Pulmo:clear,bilateral vesicular breathsounds,Unkno	
84		Physical examination	Good overall condition and nutritionalstatus, Unkn	
85		Physical examination	Head/neck normal.Normal thyroid, Unknown	
86		Physical examination	Lungs:clear on both sides, Unknown	
87		Physical examination	neurology normal,no leg edema., Unknown	
88		Physical examination	Neuro. Status:normally oriented, Unknown	
89		Physical examination	cor:heart tones pure,regular, Unknown	
90		Physical examination	No cyanosis,signs of anaemia,icterus,. Unknown	
91		Physical examination	Other abnormalities:none, Unknown	
92		Physical examination	Peripheral edema:no,pulsestatus:normal,Unknown	
93		Physical examination	no crepitations,abdomen, Unknown	
94		Physical examination	HT:2/6 systolic murmur, Unknown	
95	23-DEC-2014	Prothrombin time	110 %	130 70
96		Troponin	Elevated, Unknown	
97	10-DEC-2014	Troponin T	0.058 ng/ml	0.01 0.0
98	23-DEC-2014	Troponin T	0.042 ng/ml	0.01 0.0
99	23-DEC-2014	Troponin T	0.037 ng/ml	0.01 0.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
100	12-DEC-2014	Ultrasound abdomen	Liver homogenous.Status post CCE., Unknown	
101	12-DEC-2014	Ultrasound abdomen	Pancreas normal as far as could bedetermined., Unk	
102	12-DEC-2014	Ultrasound abdomen	DHC not dilated.Right kidneysomewhat shrunken, Unk	
103	12-DEC-2014	Ultrasound abdomen	No thickening of the intestinal wall,. Unknown	
104	12-DEC-2014	Ultrasound abdomen	Urinary bladder full.No free liquid, Unknown	
105	12-DEC-2014	Ultrasound abdomen	left kidney normal.Spleen not enlarged., Unknown	

13. Relevant Tests

Cardiac catheter examination: and T-graft to R.marg. (no clinicalevidence, Unknown
ECG: Heart axis < -30 degrees,SR,HR 76/min,LBBB, Unknown
ECG: with consecutive repolarisationdisturbance, Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	13 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	30-MAY-2012 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LAXANS /00064401/ (BISACODYL) ; Unknown

#8) SIMVABETA (SIMVASTATIN) Tablet ; Unknown

#9) TARGIN (NALOXONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE) Tablet ; Unknown

#10) VENOFER (SACCHARATED IRON OXIDE) ; 19-DEC-2012 / 01-DEC-2014

#11) AMLODIPINE (AMLODIPINE) Tablet ; Unknown

#12) CARVEDILOL (CARVEDILOL) Tablet ; Unknown

#13) CLOPIDOGREL /01220707/ (CLOPIDOGREL BISULFATE) Tablet ; Unknown

#14) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Tobacco usage and alcohol consumption were not reported. Medical history included s/p PTCA PDA of the RCA in Feb-2006, diabetic nephropathy that led to renal failure diagnosed on 19-Oct-2009, hypertrophied left ventricle, slight aortic valve stenosis, slight mitral valve insufficiency associated with distinct mitral ring calcification, and secondary normocytic normochromic anaemia. The patient was not on dialysis. The patient had no known drug hypersensitivity and no history of drug dependence. Prior to treatment with Retacrit, the

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		patient was treated with Aranesp (darbepoietin, 270 ng/kg/week, subcutaneous; dose also reported as 40 mcg every fortnight to every 4 weeks) from 06-Nov-2009 until 30-May-2012. Risk factors included coronary heart disease, hyperlipidaemia, hypertension, and diabetes type 2 with diabetic vascular complications. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Bulbitis of duodenum (Duodenitis);
Unknown to Ongoing	Relevant Med History	Gastritis erosive (Gastritis erosive);
Unknown to Ongoing	Relevant Med History	Ventricular hypertrophy (Ventricular hypertrophy);
Unknown to Ongoing	Relevant Med History	Mitral valve calcification (Mitral valve calcification);
Unknown to Ongoing	Relevant Med History	Mitral valve insufficiency (Mitral valve incompetence);
Unknown to Ongoing	Relevant Med History	Normochromic normocytic anaemia (Normochromic normocytic anaemia);
Unknown to Ongoing	Relevant Med History 19-Oct-2009	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Multiple vessel coronary artery disease (Coronary artery disease);
Unknown	Relevant Med History	Aortocoronary bypass (Coronary artery bypass);
Unknown	Relevant Med History	Cold (Nasopharyngitis);
Unknown	Relevant Med History	Appetite lost (Decreased appetite);
Unknown	Relevant Med History	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
Unknown	Relevant Med History Risk Factor	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History Risk Factor	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor	Obesity (Obesity);
Unknown	Relevant Med History	Red blood cell sedimentation rate increased (Red blood cell sedimentation rate increased);

Mfr. Control Number: 2735896

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
06-NOV-2009 to 30-MAY-2012	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	AUG	1952	62 Years	Male	62.50 kg	09	DEC	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Deep vein thrombosis [Deep vein thrombosis]

Case Description: Deep vein thrombosis. Epoetin zeta. Serious Hospira-sponsored study report from Germany , received from a physician (ref: Ge-093-0107) which refers to a 62-year-old Caucasian male patient (dry weight: 62.5 kg; height: 172 cm). The
patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 192 IU/kg week; 3 dosage/week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 24-JUN-2014 / Unknown	#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS (ACETYLSALICYLIC ACID) ; Unknown
#2) FURORESE /00032601/ (FUROSEMIDE) ; Unknown
#3) ALFACALCIDOL (ALFACALCIDOL) ; Unknown
#4) AMLODIPIN /00972401/ (AMLODIPINE) ; Unknown
#5) ENALAPRIL (ENALAPRIL) ; Unknown
#6) METOPROLOL (METOPROLOL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Since 14-Aug-2002	Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2753000

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2753000

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had glomerulonephritis leading to renal failure (first diagnosed on 14-Aug-2002) and was receiving hemodialysis since 13-May-2014 with an average of three dialysis per week. The patient had not received any other erythropoietin stimulating agents (ESA) before. The patient had no previous exposure to other biosimilars. Concomitant medications included alfacalcidol (0.5 microgram/d), Furorese (250 mg/d), metoprolol (100 mg/d), amlodipin (10 mg/d), enalapril (20 mg/d) and ASS (100 mg/d) (routes of administration not reported) , all were given for unknown indications. On 24-Jun-2014, the patient began treatment with epoetin zeta (Retacrit, lot number not available, 192 IU/kg/week, three dosages per week, subcutaneous) for renal anaemia. Informed consent for the study was obtained on 11-Nov-2014. On 09-Dec-2014, the patient developed deep vein thrombosis. Laboratory/diagnostic tests and treatment for the adverse event were not reported. There was no action taken with the suspect drug in response to the adverse event. Outcome of the adverse event was resolved on an unknown date. The reporter's opinion of causality for the event of deep vein thrombosis in relation to epoetin zeta was not assessable. Risk factors included coronary heart disease, hypertension and being a current smoker. 21-Apr-2015: Additional information received from the same reporter regarding the previous exposure of the patient to other biosimilars, concomitant medications, outcome of the adverse event, action taken with the suspect drug and opinion of causality of the reporter between the event and the suspect drug. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number and date of expiry.

Case Comment: Overall case causality: Related Event is related based on temporal relationship and medical plausibility. Suspect drug can theoretically increase the risk of thrombosis by increasing red cell concentration, but consider also contributory effects of multiple risk factors in the medical history. Follow-up: No change in previous assessment.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();
		The patient had glomerulonephritis leading to renal failure (first diagnosed on 14-Aug-2002) and was receiving hemodialysis since 13-May-2014 with an average of three dialysis per week. The patient had not received any other erythropoietin stimulating agents (ESA) before. The patient had no previous exposure to other biosimilars. Race/Ethnicity: Caucasian Risk factors included coronary heart disease, hypertension and being a current smoker.
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown	Relevant Med History Risk Factor	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor	Smoker (Tobacco user);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown	Relevant Med History Since 13-May-2014	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	01	MAR	1939	75 Years	Male	60.00 kg	14	DEC	2014	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
NSTEMI [Acute myocardial infarction]

Case Description: NSTEMI. Epoetin zeta. Serious Hospira-sponsored study report from Germany , received from a physician (ref: Ge-093-0109) which refers to a 75-year-old Caucasian male patient (dry weight: 60 kg; height: 167 cm). The patient was
enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 200 IU/kg/week 3 dosage/week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-MAY-2014 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History Since 27-Feb-2006	() Renal failure (Renal failure)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2753008

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
13-FEB-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had glomerulonephritis leading to renal failure (first diagnosed on 27-Feb-2006) and was receiving hemodialysis since 28-Feb-2012 with an average of three dialysis per week. The patient was subjected with an ESA before treatment with Retacrit. On 30-Aug-2006, the patient received Aranesp (darbepoetin alfa, 333.3 ng/kg/week, route of administration not reported) for an unknown indication. Concomitant medications were not reported. On 21-May-2014, the patient began treatment with Retacrit (epoetin zeta, 200 IU/kg/week, three dosages per week, subcutaneous, lot number not reported) for renal anaemia. Informed consent for the study was obtained on 12-Nov-2014. On 14-Dec-2014, the patient developed NSTEMI. Laboratory/diagnostic tests and treatment for the adverse event were not reported. Action taken with the suspect drug was not reported. Outcome of the adverse event was recovered without sequelae on 25-Dec-2014. The reporter's opinion of causality for the event of NSTEMI was not reported.
Risk factor included hypertension. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, previous exposure of patient to other biosimilars. 25-Feb-2015: Corrected report was created to reflect the event cessation date as 25-Dec-2014 (instead of 25-Dec-2015) in the corresponding data field.

Case Comment: Overall case causality: Related Event is related based on temporal relationship and medical plausibility. Suspect drug can theoretically increase the risk of thromboembolic events by increasing red cell concentration. - N. Gonzales (20 Feb 2015) Corrected report: No change in previous assessment. - N. Gonzales (25 Feb 2015)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. The patient had glomerulonephritis leading to renal failure (first diagnosed on 27-Feb-2006) and was receiving hemodialysis since 28-Feb-2012 with an average of three dialysis per week. The patient was subjected with an ESA before treatment with Retacrit. On 30-Aug-2006, the patient received Aranesp (darbepoetin alfa, 333.3 ng/kg/week, route of administration not reported) for an unknown indication. Race/Ethnicity: Caucasian Risk factor included hypertension.
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History Since 28-Feb-2012	Hemodialysis (Haemodialysis);
Unknown	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	28	FEB	1943	71 Years	Male	78.00 kg	15	MAY	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Septic shock [Septic shock]
Stroke [Cerebrovascular accident]

Case Description: Fatal septic shock and stroke. Epoetin zeta. Serious Hospira-sponsored clinical study report from Greece, received from an investigator, which refers to a 71-year-old Caucasian male patient (Gr-003-0024; weight: 78 kg, height: 168 cm).
The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 13-SEP-2014
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 6000 IU, Freq: 1 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 13-FEB-2014 / 13-SEP-2014

19. THERAPY DURATION
#1) 213 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) COAPROVEL (HYDROCHLOROTHIAZIDE, IRBESARTAN) ; Unknown / 13-SEP-2014
#2) FERROSANOL (FERROUS GLYCINE SULFATE) ; Unknown / 13-SEP-2014
#3) FILICINE (FOLIC ACID) ; Unknown / 13-SEP-2014
#4) FOSRENOL (LANTHANUM CARBONATE) ; Unknown / 13-SEP-2014
#5) LIPITOR (ATORVASTATIN CALCIUM) ; Unknown / 13-SEP-2014
#6) SALOSPIR (ACETYLSALICYLIC ACID) ; Unknown / 13-SEP-2014

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2819938

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-MAR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was an ex-smoker (type and quantity not reported). He had no history of drug hypersensitivities and drug dependence. Medical history included hypertensive nephropathy which led to renal failure diagnosed on 10 Nov 2010 (also reported as 2011), stroke (2002 and 2003), and hypertension (1994). The patient was not on dialysis. The patient has not been treated with an erythropoiesis-stimulating agent (ESA) nor had received Retacrit prior to the study. Concomitant medications included Lipitor (20 UOM not reported, once a day) for hyperlipidemia, Zemplar (1 UOM not reported, once a day) for osteodystrophia, Ferrosanol (1 UOM not reported, once a day) for anemia, Filicine (1 UOM not reported, once a day) for anemia, Coaprovel (300+12.5 UOM not reported, once a day) for hypertension, Zylapour (300 UOM not reported, once a day) for UA, Salospir (100 UOM not reported, once a day) for stroke, and Fosrenol (800 UOM not reported, thrice a day) for increased P serum (routes of administration not reported). On 13 Feb 2014, the patient began treatment with epoetin zeta (Retacrit; 6000 IU, once a week, with a mean dose of 76.9 IU/kg/week, subcutaneous; lot number not reported) for renal anaemia. On 15 May 2014, the patient experienced stroke. There were no relevant tests conducted. Treatment was not reported; however, the patient was admitted to the hospital on the same date because of the event. There was no action taken with Retacrit in response to the event. On the same day of 15 May 2014, the patient has recovered with sequelae from stroke and was discharged from the hospital. On an unknown date, the patient experienced septic shock. Treatment was not reported; however, the patient was admitted to the hospital on 10 Sep 2014 because of the event. The patient died on 13 Sep 2014. Cause of death was septic shock. It was not reported if autopsy was performed. The investigator considered the events not related to Retacrit. Risk factors included stroke, hypertension and smoking. 22 Jul 2015: Additional information was received from the investigator. Additional event fatal septic shock was reported. Previously reported thromboembolic events was updated to stroke; event details including onset date, outcome, and causality were provided. Seriousness criterion was changed from other medically important condition to life threatening and death . Suspect drug information including action taken in response to the event was provided; dose was updated to 6000 IU (previously reported as mean dose 76.9 IU/kg/week). Patient age was reported. Patient weight was updated to 78 kg (previously 77 kg). Onset dates of the patient's medical history were provided. Concomitant medications were provided. This information has been incorporated in the narrative and the corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: lot number, date of expiry, and previous exposure of patient to other biosimilars. 04-Sep-2015: Additional information was received from the investigator. Stroke was updated to a fatal adverse event. This information has been incorporated in the narrative and corresponding data fields. 07-Mar-2016: Additional information received from the investigator. Outcome of stroke was updated to recovered with sequelae (previously reported as fatal). This information has been incorporated in the narrative and the corresponding data fields.

Case Comment: Overall case causality: Possible (reporter causality not reported) Hospira causality: Not assessable Cannot provide causation without firm timeline, objective clinical event details, pertinent laboratory findings and concomitant medications. Follow-up: Overall case causality: Not assessable Fatal septic shock and stroke are not assessable. While risk factors are noted, cannot provide definitive assessment without further objective clinical event details and pertinent laboratory test results (including post-mortem findings for the fatal event). Follow-up: No change in assessment. Follow-up: No change in previous assessment. The stroke still cannot be assessed without further objective clinical event details. While the drug can theoretically increase the risk of thromboembolic events, it was unclear if the stroke was thrombotic or hemorrhagic in nature.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ZEMPLAR (PARICALCITOL) ; Unknown / 13-SEP-2014

#8) ZYLAPOUR (ALLOPURINOL) ; Unknown / 13-SEP-2014

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol use was not reported. The patient was an ex-smoker (type and quantity not reported). He had no history of drug hypersensitivities and drug dependence. Medical history included hypertensive nephropathy which led to renal failure diagnosed on 10 Nov 2010 (also reported as 2011), stroke (2002 and 2003), and hypertension (1994). The patient was not on dialysis. The patient has not been treated with an erythropoiesis-stimulating agent (ESA) nor had received Retacrit prior to the study. Race/Ethnicity: Caucasian The patient died on 13 Sep 2014. Causes of death were septic shock and stroke. It was not reported if autopsy was performed.

Mfr. Control Number: 2819938

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History Diagnosed 10 Nov 2010 (also reported as 2011)	Renal failure (Renal failure);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History Risk Factor - 1994	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor - 2002, 2003	Stroke (Cerebrovascular accident);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	11	AUG	1938	76 Years	Female	72.00 kg	20	FEB	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Chronic kidney disease [Chronic kidney disease]
Infection [Infection]
Multiple organ failure [Multiple organ dysfunction syndrome]
Myocardial infarction (NSTEMI) [Acute myocardial infarction]

Case Description: Fatal chronic kidney disease, fatal infection, fatal multiple organ failure and myocardial infarction (NSTEMI). Epoetin zeta. Hospira-sponsored study report received from an investigator (ref: Sw-005-0030) which refers to a patient (height:
165 cm, dry weight: 72 kg).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 05-APR-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 55.55 IU/k (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low HB (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 21-MAR-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2830712

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had lithium nephropathy leading to renal failure (first diagnosed on 29-Oct-1984) and was receiving hemodialysis since 25-Jan-2012 with an average of three dialysis per week. The patient was treated with an erythropoietin stimulating agents (ESA) before treatment with Retacrit. From 13-Apr-2006, also reported as 23-Apr-2008, until 21-Mar-2012, the patient received epoetin beta (Neorecormon, 55.55 IU/kg/week, mean dose reported as 4000, route of administration not reported). It was reported that the patient did not experience any thromboembolic event during treatment with any other ESA. Medical history included hyperlipidaemia and ischemic heart disease. Concomitant medications were not reported. On 21-Mar-2012, also reported as 05-Dec-2014, the patient began treatment with epoetin zeta (Retacrit, 55.55 IU/kg/week, one dosage per week, subcutaneous; batch number not known) for low HB. The patient was enrolled in the study on 07-May-2014. On 04-Feb-2015, the patient's haemoglobin was 116 g/L (normal values: 117-153). On 20-Feb-2015, the patient was admitted to the hospital because of myocardial infarction (NSTEMI). On 21-Feb-2015, the patient's haemoglobin was 123 g/L. On an unknown date, the patient developed multiple organ failure due to renal failure due to chronic kidney disease. On 04-Mar-2015, the patient had an atrial fibrillation. Treatment for the event of NSTEMI included CABG on 06-Mar-2015. However, it was reported that the last dose of Retacrit prior to the events was given on 25-Feb-2015. Investigations on 20-Mar-2015 at 05:00 am, revealed haemoglobin at 91 g/L and platelets at 240 x10^9/L (normal values: 160-390); on 21-Mar-2015 at 04:30 am, the patient's haemoglobin was 89 g/L, platelets of 280 x 10^9/L and PK-INR of 1.2 (normal values: 0.8-1.2); and on 30-Mar-2015 at 06:00 am, the patient's haemoglobin was 84 g/L and platelets of 135 x 10^9/L. Outcome of the event of myocardial infarction (NSTEMI) was not recovered at the time of the report. The patient died on 05-Apr-2015. Cause of death was reported as multiple organ failure due to infection due to chronic kidney disease. It was not reported if an autopsy was performed. The reporter's opinion of causality for the event of multiple organ failure due to infection due to chronic kidney disease in relation to Retacrit was not related, while unlikely for the event of mycoradial infarction (NSTEMI). Risk factors included stroke, hypertension and antithrombin III deficiency which started on 08-Mar-2015. 24-Sep-2015: Additional information received from the same reporter. Myocardial infarction (NSTEMI) was added as an adverse event. Patient's day of birth, age; and laboratory test were provided. Therapy start dates of epoetin zeta and epoetin beta were also reported as 05-Dec-2014 and 23-Apr-2008 respectively. Indication of epoetin zeta was updated to low HB (previously reported as renal anaemia). Death date was updated to 05-Apr-2015 (previously reported as 04-Apr-2015). Hospitalization and life threatening were added as seriousness criteria. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product, Retacrit: batch number, date of expiry and previous exposure of patient to other biosimilars. 02-Oct-2015: Received English translation of Swedish text. Additional information also received from the same reporter. Treatment and reporter's opinion of causality for the event of myocardial infarction (NSTEMI) were provided. Laboratory tests performed on March 20, 21 and 30 year 2015 were also provided. Antithrombin III deficiency was added as a risk factor. Hyperlipidaemia and ischemic heart disease were added as medical history. Atrial fibrillation on 04-Mar-2015 was reported as a concurrent disease. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Not related Noting the reporter's assessment, the nature of the adverse events and the underlying medical conditions, consider events to be due to natural progression of the patient's infection, with contributory effects from underlying renal condition. Suspect drug has no known immunosuppressive effects. Follow-up: Overall case causality: Related The newly added adverse event of myocardial infarction is possibly related as this is a labeled event for the suspect drug. Retacrit can theoretically increase the risk of thromboembolic events. Consider possible contributory effects of preexistent cardiovascular risk factors. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	04-FEB-2015	Haemoglobin	116 g/l	
2	21-FEB-2015	Haemoglobin	123 g/l	
3	20-MAR-2015	Haemoglobin	91 g/l	
4	21-MAR-2015	Haemoglobin	89 g/l	
5	30-MAR-2015	Haemoglobin	84 g/l	
6	21-MAR-2015	International normalised ratio	1.2 , Unknown	
7	20-MAR-2015	Platelet count	240, X10**9/L	

Mfr. Control Number: 2830712

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
8	21-MAR-2015	Platelet count	280, X10**9/L	
9	30-MAR-2015	Platelet count	135, X10**9/L	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	55.55 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Low HB (Haemoglobin decreased)	21-MAR-2012 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. The patient had lithium nephropathy leading to renal failure (first diagnosed on 29-Oct-1984) and was receiving hemodialysis since 25-Jan-2012 with an average of three dialysis per week. The patient was treated with an erythropoietin stimulating agents (ESA) before treatment with Retacrit. From 13-Apr-2006, also reported as 23-Apr-2008, until 21-Mar-2012, the patient received epoetin beta (Neorecormon, 55.55 IU/kg/week, mean dose reported as 4000, route of administration not reported). It was reported that the patient did not experience any thromboembolic event during treatment with any other ESA. Medical history included hyperlipidaemia and ischemic heart disease. Race/Ethnicity: Caucasian The patient died on 05-Apr-2015. Cause of death was reported as multiple organ failure due to infection due to chronic kidney disease. It was not reported if an autopsy was performed. Risk factors included stroke, hypertension and antithrombin III deficiency which started on 08-Mar-2015.
Unknown to Ongoing	Relevant Med History Started on 08-Mar-2015	Hyperlipidaemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Nephropathy (Nephropathy);
Unknown to Ongoing	Relevant Med History first diagnosed on 29-Oct-1984	Renal failure (Renal failure);
Unknown	Relevant Med History Risk Factor-Started on 08-Mar-2015	Antithrombin III deficiency (Antithrombin III deficiency);
Unknown	Relevant Med History Risk Factor	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History Risk Factor	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History since 25-Jan-2012 with an average of three dialysis per week	Hemodialysis (Haemodialysis);
13-APR-2006 to 21-MAR-2012	Past Drug Event	EPOETIN BETA (EPOETIN BETA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	17	APR	1950	64 Years	Male	81.00 kg	24	MAR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Nontransmural myocardial infarction [Myocardial infarction]
Thromboembolic event [Embolism]

Case Description: Nontransmural myocardial infarction and thromboembolic event. Epoetin zeta. Hospira sponsored study report received from an investigator (ref: Bg-004-0022) which refers to a patient.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Drug use for unknown indication (Produ
(Continued on Additional Information Page)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 01-MAR-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2846883

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-DEC-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2846883

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-
Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included diabetic nephropathy which led to the diagnosis of renal failure in Sep-2010. The patient had been treated with an Erythropoesis Stimulating Agent (ESA) epoetin beta (Neorecormon, 111 IU/kg/week; route of administration not reported) for an unknown indication in 2011. The patient was not on dialysis. Concomitant medications were not reported. On an unknown day in Mar-2013, prior to enrollment to the study, the patient started to receive treatment with epoetin zeta (Retacrit, subcutaneous; dose not reported) for an unknown indication. On 24-Feb-2014, the patient was enrolled in the study and signed informed consent. During week of enrollment, the patient received epoetin zeta (Retacrit, 111 IU/kg/week, subcutaneous, 3 dosages per week; lot number unknown) for renal anaemia. On 24-Mar-2015, the patient experienced nontransmural myocardial infarction. Then on 09-May-2015, the patient had a thromboembolic event. Laboratory or diagnostic tests, treatment, action taken with the suspect drug in response to the adverse events, and outcome were not provided. It was reported that the patient was alive and was feeling well. At the time of the report, the patient was on HD three times weekly. It was also reported that from 14-May-2015, the epo treatment will be changed from Retacrit to Binocrit. The reporter's opinion of causality between the events and the suspect drug was not provided. Risk factors included coronary heart disease, hypertension, diabetes type 2 with vascular complications and heart failure NYHA stage II. 13-May-2015: Additional information was received from another investigator. Alternative therapy was provided. It was reported that the patient was alive and was feeling well, and was on hemodialysis three times a week at the time of the report. This information has been incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit (epoetin zeta): lot number, date of expiry, and previous exposure of patient to other biosimilars. 04-Jun-2015: Additional information was received from the same investigator to update adverse event onset date to 24-Mar-2015 (previously reported as 22-Mar-2015). This has been incorporated in the narrative and in the corresponding data fields. 11-Dec-2015: Additional information was received from the same reporter. Thrombolic event was added as an adverse event. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Related Event is related based on temporal relationship and medical plausibility. Patient had been using the medication for almost two years. Retacrit can theoretically increase the risk of thromboembolic events such as myocardial infarction. Consider also contributory effects from pre-existent risk factors. Follow-up: No change in previous assessment. Follow-up: No change in previous assessment. Follow-up: No change in assessment of previous event. New event with the same causality.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	UNK; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	01-MAR-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #2	111 IU/kg/week, Freq: 3 Week; Interval: 1; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to the diagnosis of renal failure in Sep-2010. The patient had been treated with an Erythropoesis Stimulating Agent (ESA) epoetin beta (Neorecormon, 111 IU/kg/week; route of administration not reported) for an unknown indication in 2011. Risk factors included coronary heart disease, hypertension, diabetes type 2 with vascular complications and heart failure NYHA stage II. Race/ Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);

Mfr. Control Number: 2846883

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
01-JAN-2011 to Unknown	Past Drug Event Lot Number: [UNK]	NEORECORMON (NEORECORMON); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
PRIVACY	ITALY	26	MAR	1942	72 Years	Female	51.00 kg	21	FEB	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pure red cell aplasia [Aplasia pure red cell]
Lack of efficacy [Drug ineffective]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11, regarding subject 1160032.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S017S4; Exp.Dt. 01-NOV-2016}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 100 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)
(Continued on Additional Information Page)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DEURSIL (URSODEOXYCHOLIC ACID) Tablet ; Unknown
#2) PANTORC (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown
#3) TRANSTEC (BUPRENORPHINE) Transdermal patch ; Unknown
#4) BISOPROLOL (BISOPROLOL) Tablet ; Unknown
#5) CARDIRENE (ACETYLSALICYLATE LYSINE) Tablet ; Unknown
#6) DELORAZEPAM (DELORAZEPAM) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1990 to Ongoing	Relevant Med History	Acute pyelonephritis (Pyelonephritis acute)
Unknown to Ongoing	Relevant Med History	Ischaemic cardiomyopathy (Ischaemic cardiomyopathy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2876300

24c. DATE RECEIVED BY MANUFACTURER
23-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

25b. NAME AND ADDRESS OF REPORTER
Dr. Vincenzo Panichi
Dept: Department of Nephrology and Dialysis, Versilia Hospital
Via Aurelia 335
Lido di Camaiore, LU 55043
ITALY

NAME AND ADDRESS WITHHELD.

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Hospira-sponsored study report received from an investigator (ref: It-116-0032). This report was also received from AIFA (ref: IT-MINISAL02-314141). Subject was enrolled in Hospira-Sponsored Post Authorization Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for treatment of renal anemia. Subject had no known drug hypersensitivities or history of drug dependence, no exposure to interferon and ribavirin. She was not pregnant or lactating at time of the report. She had unilateral kidney surgery which led to renal failure in 1990. She had no family history of hypertension, type 2 diabetes mellitus, or nephropathy. She was a non-smoker and had a one pregnancy to term. Subject had a history of relapsing renal colic with calculus issuing never analyzed. In 1990, Subject underwent L nephrectomy through severe urolithiasis complicated by acute pyelonephritis and severe sepsis. On discharge Subject reported slight renal failure. During same admission underwent some blood transfusions w/subsequent acute hepatitis B. In 1991, Subject had surgical removal of voluminous calculus R kidney followed by ESWL. In 1995, Subject underwent positioning of right nephrostomy for obstructive urolithiasis and subsequent resolution. In 2006, Subject has been diagnosed with hypertension. In 2007, Subject was diagnosed with STEMI, and in regular follow-up at the time of the report. In Jun2014, onset of severe coxalgia treated with anterior radiation of groin, followed by right gonalgia for which x-rays of pelvis, lumbosacral spine were performed. Subject had lumbosacral CT and orthopaedic visit. There was subsequent persistence of pain and notable functional limitation evaluated at antalgic therapy day hospital, wherein Depalgos was prescribed and three infiltrations of R knee were performed. Subject was not treated w/Erythropoiesis-Stimulating Agent (ESA) prior to treatment with Retacrit. Subject was not on dialysis. Concurrent diseases included single R kidney surgery for L nephrolithiasis complicated by acute pyelonephritis, chronic ischemic cardiomyopathy w/moderate mitral regurgitation, severe R coxarthrosis, colonic diverticulosis, hiatal hernia and lower UTI. Concomitant medications included bisoprolol 1.25 mg tablet, simvastatin 20 mg tablet, Pantorc 40 mg, ursodeoxycholic acid 450 mg tablet, folic acid 5 mg tablet, sodium bicarbonate 500 mg, delorazepam drops, Cardirene 75 mg tablet, Transtec 35 mcg, piperacillin/tazobactam 2 g.

17Jun2014 Subject began treatment with epoetin zeta (Retacrit, lot numbers: 4S017S4, 4T051U4, 4V067V4, 4S033X4; 100 IU/kg, 1 dose/week, daily dose reported as 4000 x 3/week and 3 IU in thousands weekly, subcutaneous, lot number unknown) for renal anemia. Subject was self-administering at home, started on same date of 17Jun2014. Subject lived in a village where Retacrit was provided for inhabitants. Subject had been informed and trained about storage conditions and how to administer Retacrit at beginning of treatment. Subject was very compliant to instruction given.

Dec2014 Subject was admitted in hospital department for reassessment. Some doses were administered when subject was hospitalized. No antibody or blood samples were taken from subject on entry in study or prior to study drug administration. Laboratory tests and diagnostic procedure in Dec2014 included sCR 3.7 mg/dl (normal range 0.4-1.1), Hb 10.2 g/dl (12-16), abdominal ultrasound exam within normal apart from R kidney w/reduced cortex finely irregular margins with moderate caliectasis. On unknown date, tests included heart echo which showed systolic function conserved w/moderate mitral regurgitation, chest x-ray showed pleural issues to R to be investigated further with chest CT. R hip X-ray showed severe coxarthrosis w/coarse subchondral cysts. Subject had orthopaedic visit which revealed possible aseptic necrosis of hip to be investigated further using MRI or CT (second choice). With presence of metal clips at site of previous L nephrectomy it was not possible to study coxarthrotic framework with MRI and Subject was referred to Orthopaedics. Pancolonoscopy as day subject was recommended given presence of continually positive SOF. On 21Feb2015, subject presented to accident and emergency with intense asthenia and slight dyspnea. On same day, subject developed severe anemia due to unresponsive treatment to ESA reported as lack of effect, and was suspected of aplasia pure red cell (PRCA). Subject was subject to diagnostic verification with chronic severe renal failure (NKF stage IV-V). Laboratory tests on same day included Hb 3.9 g/dl (also reported as mg/dl), and sCr 3.7 mg/dl, 6 blood transfusions were performed. On 25Feb2015, subject was admitted to hospital. On same day, sCr 3.5 mg/dl, Hb 10.6 - 9.3 g/dl and Htc 31% (normal range 37-47), serum iron 227 mcg/dl, transferrin 201 mg/dl, ferritin 268 ng/dl, and normal electrophoretic pattern. On same day, ECG showed sinus bradycardia, T-wave negative/biphasic in lower ranges. On 02Mar2015 pancolonoscopy exam conducted up to cecum in conditions of poor intestinal cleansing allowing only exclusion of coarse mucosal lesions, multiple diverticula in descending-sigmoid colon. Z-line with salmon-coloured mucosal stria running up from there for 15 mm (biopsies), LES hypotonic, stomach within normal, hiatal hernia. Barrett's metaplasia can be excluded. Histology exam showed gastroesophageal junction w/moderate non-specific phlogosis within its flap. On 05Mar2015, chest CT revealed cavitary formation of around 5 cm maximum diameter w/walls w/irregular thickening associated w/solid satellite nodules less than 1 cm tending to converge in subpleural region of posterior basal segment of lower L lobe; this lesion communicates w/subsegmental bronchus of basal posterior area. GGO nodule less than 1 cm in upper R lobe. Some bilateral micro nodules currently not able to be characterised given negligible and insignificant scale. Bibasiliar disventilatory fibrotic stria. Ectasia of ascending aorta (around 4 cm); coronary calcification. Small (maximum short radius less than 1 cm) mediastenic lymph nodes in absence of pathological adenomegalies. Outcomes of L nephrectomy w/post-laparoptic hernia of lateral abdominal wall w/herniated colon. R kidney w/thinning of cortex and cortical cysts. Required completion with bronchoscopy w/BAL in first instance. On 09Mar2015 subject underwent bronchoscopy w/no lesions detectable endoscopically within explorable areas. BAL performed on R inferior lobar bronchus; same characteristics on L. Hgb values remained stable during admission. Dosage regimen of acetylsalicylic acid and increased supplementation with erythropoietin. No evident cause of anemia arose from exams performed. Performed chest CAT and bronchoscopy w/BAL (culture and cytology exam not reported). On 10Mar2015 subject discharged from hospital w/pending performing R hip prosthesis intervention. Tests at discharge showed Hb 9.3 and Htc 26.5. On 25Mar2015 erythrocyte 2.82 x 10e6/ mcl (normal range 4.2- 5.4), Hgb 8.1 g/dl (also reported as 8 g/dl), Hct 22.6 %, creatinine 3.85, MCV 80.1 fl (81-99), MCH 35.8 g/dl (31-35), RDW 14% (11.5-14.5). On 08Apr2015 erythrocyte 2.18 x 10e6/ mcl, Hgb 6.2 g/dl, Hct 17.6%, MCV 80.7 fl, MCH 35.2 g/dl, RDW 14.3%. One blood transfusion was done to subject 08Apr2015. On 09Apr2015 subject again admitted to hospital. On same day, ECG showed sinus rhythm and RAV grade 1. Tests on admission showed Hb 7.3 g/dl, sCr 3.7 mg/dl, hematocrit 21 fl, MCV 83 fl, reticulocyte count 0.1 %, esophagogastroscopy (result not reported). On 10Apr2015 x-ray R hip and R femur revealed notable R coxarthrosis w/coarse subchondral cysts of femoral head and bone rarefaction on internal face of femoral head, vascular calcification. On 13Apr2015 pancolonoscopy showed sigmoid w/lumen deformed by widespread diverticulosis and perivisceral inflammation, colon affected by hernia following L nephrectomy. Having passed this section with difficulty, reached cecum

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

w/out finding legions of colonic segments. Ileocecal valve visible. Conclusion: sigmoid diverticulosis, sigmoid perivisceral inflammation. On 15Apr2015 abd US showed liver dimensions w/in limits w/regular margins, surface, profiles and structure, affected by focal lesions. Cholecystolithiasis, expanded in spite of recent meal, w/regular walls. At infundibular and first biliary duct level, thickening of walls and endoluminal material not visible to ultrasound (biliary sludge). Broad bile duct up to pancreas w/out obstructing endo or extra luminal images. Hepatic portal vein within limits. Suprahepatic veins regular. Non-visible pancreas affected by focal lesions in visible segments. Pancreatic duct regular; spleen small (diameter 90 mm). Aorta and 'illegible' with widespread fibrocalcification affected by aneurysmal lesions. Vena cava patent within limits. R kidney in situ large through vicarious hypertrophy (diameter 120 mm), w/parenchymal ring reduced by some corticalised calyces. Papillary plaques, non-calculus, no signs of obstructive uropathy. No expansion of adrenal cavities; bladder half empty w/no flow of liquid between intestinal loops. Exams performed during admission showed hypo-regenerative anemia which never responded to increase of dosage of EPO implemented around one month from time of report, in conditions of adequate iron reserves. In light of non-diagnostic pancolonscopy exam, Subject underwent another endoscopy, w/negative result and bone marrow biopsy to better clarify bone marrow situation. On an unknown date, bone marrow biopsy revealed 20% cellular, reticulum thickened, increased of colorable deposits, lymphocytes 8% insterstitial and in small B and T aggregates, 5% polytipycal plasma cells markedly hypoplasic erythroid series, hyperplasia of megacariocyte and granulocyte line with evidence of eosinophils series and CD34 blasts less than 5%. On 16Apr2015 subject discharged from hospital. Tests on discharge showed creatinine (sCr) 3.1, Hb 9.6, Hct 27.4, MCV 82. 5. On 21Apr2015 erythrocyte 3.36 x10e6/ mcl, Hgb 9.7 g/dl, Hct 28.2%, MCV 83.9 fl, MCH 34.4 g/dl, RDW 13.6%. On 30Apr2015 erythrocyte 2.97 x10e6/ mcl, Hgb 8.5 g/dl, Hct 24.7%, MCV 83.2 fl, HCH 34.4 g/dl, RDW 13.5%. On 12May2015 erythrocyte 2.47 x10e6/ mcl, Hgb 7.1 g/dl, Hct 20.3%, MCV 82.2 fl, MCH 35 g/dl, RDW 13.4%. On 18May2015 erythrocyte 2.25 x10e6/ mcl, Hgb 6.4 g/dl, Hct 18.6%, MCV 82.7 fl, MCH 34.4 g/dl, RDW 13.6%. Two blood transfusions done on 18May2015. On 18May2015 therapy w/epoetin zeta withdrawn and subject also withdrawn from study. On 18Jun2015 and 23Jun2015, two blood transfusions were done. Antibodies against erythropoietin in serum samples confirmed with titer of 1:40,960 collected on 03Jul2015; 1:81,920 collected on 29May2015; and 1:40,960 collected on 03Jul2015, as determined by an RIP assay. Neutralizing antibodies (NAB) detected positive in all 3 samples usingcell based functional assay. Subject had no improvement after drug was withdrawn. Treatment included blood transfusion and administration of steroids. Event resolved on unknown date with use of steroids alone. Subject was doing well; no more blood transfusion and Hb 10 gr/dL at time of report. Suspect drug was not re-administered. The investigator's causality opinion between adverse event of pure red cell aplasia and suspect drug was not reported. Myocardial infarction and hypertension were considered risk factors. 29May2015: Corrected report created to change subject's age to 72.
01Jun2015: English translation of Italian report received. Follow-up report was created to reflect updates regarding subject's medical history and diagnostic procedures. Subject's diagnosis, date of withdrawal from study, and previous exposure to other biosimilar (previously not reported) were also added. Bisoprolol, simvastatin, Pantorc, ursodeoxycholic acid folic acid, sodium bicarbonate, delorazepam drops, Cardirene, Transtec, piperacillin/tazobactam added as concomitant medications. This information has been incorporated in narrative and in corresponding data fields.
01Jul2015: Additional information was received from AIFA (ref: ITMINISAL02- 314141). Aplasia pure red cell added as adverse event. Ethnicity reported as European. Route of administration of bisoprolol, simvastatin, Pantorc, ursodeoxycholic acid, folic acid, sodium bicarbonate, delorazepam drops, Cardirene was updated to oral. Reticulocyte count and esophagogastroscopy added as tests. Dose of epoetin zeta also reported as 3 IU in thousands weekly. Subject had no improvement after drug withdrawn and that drug was not readministered. Information incorporated in narrative and corresponding data fields. Data entry correction was also made to reflect event of severe anemia was reported as lack of effect; and to reflect date tests in the data field. Reporter unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: presentation.
08Jul2015: Additional information received from same reporter. No antibody or blood samples taken from subject on entry in study. Subject also had no exposure to interferon or ribavirin. Tests on 25Feb2015 included serum iron, transferrin and ferritin, electrophoretic pattern. Subject was transfusion-dependent at time of report. Blood transfusions done on 08Apr2015, 18May2015, 08Jun2015, and 23Jun2015.
17Jul2015: Additional information received from another reporter regarding positive detection of neutralizing antibodies (NAB) against erythropoietin in all 3 serum samples collected.
03Aug2015: Additional information received from another reporter. Lot numbers of epoetin zeta received by subject added. Subject was self-administering at home.
01Sep2015: Additional information received from the same reporter. First home administration of Retacrit of subject was on 17Jun2014.
28Sep2015: Additional information received from same reporter.
17Nov2015: Clarification received from same reporter. Adverse event was updated to pure red cell aplasia from aplasia pure red cell and anemia severe, was hospitalized.
23Dec2015: Additional information received from reporter. Outcome of pure red cell aplasia updated to resolved (previously ongoing).

11Feb2016: Additional information received from reporter. Previously reported lack of efficacy was added as adverse event.

Follow up (10May2016): This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up CIOMS I or MedWatch report may indicate in the appropriate field that it is an initial report.
Subject's condition stable, good w/Hb 9 g/dl. Subject receiving neither transfusions nor treatment with epo. Reporter believed that AB levels were reduced.

Follow-up (30May2016): This is a follow-up report to notify that the case 2016269740 and 2876300 are duplicates. All subsequent follow-up information will be reported under manufacturer report number 2876300. New information from a literature report from the Clinical Kidney Journal, 2016,9 (2); 1-4 entitled Pure red cell aplasia induced by epoetin zeta includes:
72yo Caucasian female regularly followed up in Nephrology Outsubject Clinic because of slowly progressive CKD. In 1990 subject

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

underwent L nephrectomy for severe nephrolithiasis, complicated by acute pyelonephritis and sepsis. In 1991, she developed new stones in the right kidney and received extracorporeal shock wave lithotripsy. In 1995 right nephrostomy was put in place because of obstructive nephrolithiasis. In 2006 hypertension was detected. In 2007 she had acute myocardial infarction. Since then, she has been under regular cardiologic follow- up. From 2007 until 2014 kidney function slowly deteriorated, reaching stage IV-V CKD. In June 2014, she attended the Day Hospital of the Nephrology Unit for severe hip arthrosis. Her (Hb) was 9.7 g/dL with adequate iron stores; she was prescribed epoetin zeta 4000 IU twice a week subcutaneously and antalgic therapy for hip pain. In Dec2014, she was hospitalized for 4 days in the Nephrology Department due to the persistence of severe hip pain. The subject's serum creatinine was 3.7 mg/dL and Hb was 10.2 g/dL. Given that occult blood was detected in three stool samples, colonoscopy was suggested. In Feb2015, the subject arrived at the Emergency Unit because of severe asthenia and mild shortness of breath. On 25Feb2015, her Hb was 3.9 g/dL and 9.3 g/dl post transfusion, reticulocytes were not available, leucocytes were 6850 N/mmc, platelet count was 136000 (no units provided), serum iron was 227 ug/dl, transferrin saturation was 80.5 percent (post transfusion), serum ferritin was 268 ng/ml, serum creatinine was 3.5 mg/dl, c-reactive protein was not available and parathyroid hormone was not available. She received blood transfusion (six units of packed red cells) and was admitted again to the Nephrology Department. Unremarkable findings were obtained from chest computed tomography, bronchoscopy and upper endoscopy. Colonoscopy showed diverticulosis, but was not diagnostic for incomplete cleaning. At 2 weeks after admission, at discharge her Hb was 9.3 g/dL; epoetin zeta dose was increased to 4000 IU three times per week. In April 2015, she was hospitalized again for 8 days because of severe anemia (Hb 6.2 g/dL, reticulocytes 0.1%, 2500/µL). Colonoscopy was repeated confirming known diverticulosis. Abdomen ultrasound was unremarkable for possible causes of anemia. The subject underwent bone marrow biopsy showing severe hypoplasia of the erythroid line (CD34 blasts <5%) with hyperplasia of the megakaryocytic and granulocytic lines. In May 2015, at the time when bone marrow biopsy became available, the subject had become transfusion dependent and epoetin zeta administrations were immediately interrupted. Assays for antinuclear Ab, anti-DNA Ab and hepatitis B Ab were normal; Parvovirus B19 DNA and hepatitis B antigen were not detected. Anti-EPO Ab were tested and found positive in three different samples by a screening assay, followed by specificity confirmation testing. These were anti-EPO neutralizing Ab (titre of 1:81 920). She was then diagnosed with anti-EPO-mediated PRCA. The subject was prescribed oral prednisone (0.5 mg/kg/day) for 3 months and progressive decrease in the need for blood transfusions was observed. In September 2015, she received her last blood transfusion and steroid therapy was interrupted. Since then, her Hb values have stabilized (last available Hb value of 11.5 g/dL in February 2016). No worsening of renal function had occurred over the period (in February 2016, serum creatinine was 3.9 mg/dL). Retesting of anti-EPO Ab titre has already been planned, in the case the subject needs re-challenging with ESA in the future. The severity of anaemia, which had become unresponsive to ESA therapy, was testified by the very low reticulocyte count and by the dependence on blood transfusions. The platelet and granulocyte counts were normal. PRCA diagnosis was supported by the findings of the bone marrow biopsy, showing severe hypoplasia of the erythroid line, and by the presence of high-titre anti-EPO neutralizing Ab. No other causes of PRCA, such as Parvovirus or hepatitis B infection, thymoma, lymphoproliferative disorders, drugs or autoimmune disease were identified. PRCA has also been reported in subjects with no underlying disease. However, the timing from drug exposure and the fact that the subject received uniquely epoetin zeta makes the relationship between the drug and the occurrence of PRCA extremely likely. PRCA has been described to occur with all ESA. Considering its rarity, it is difficult to distinguish whether this is a sporadic case or the expression of increased immunogenicity of epoetin zeta. The calculation of PRCA incidence based on length of exposure to epoetin zeta would be of interest, but is beyond the scope of this case report. Various immunosuppressive strategies have been used to cure PRCA. However, in the absence of randomized clinical trial, there are insufficient data to provide guidance on the preferred immunosuppressive agents or treatment regimen. The subject obtained remission from PRCA following therapy with steroids. This is in line with other reports in the literature. This conservative strategy was chosen considering her age and comorbidities. Interestingly, after therapy her Hb stabilized without the need to challenge her with new ESA therapy. It is possible that the iron load she received with blood transfusion had contributed to Hb stability after the recovery of PRCA. One possible limitation of this case report is that reticulocytes were not tested at onset and that PRCA diagnosis was made with a certain delay. While this does not reduce the importance of the relationship between epoetin zeta use and the occurrence of PRCA, it was acknowledged that an earlier testing of reticulocyte values would have prevented needless workup of anaemia with endoscopies and CT scans, and directed them towards bone marrow biopsy sooner. A more timely diagnosis would also have prevented the increase in epoetin zeta dose, which have possibly enhanced anti-EPO Ab production. To conclude, we report for the first time a subject who developed Ab-mediated PRCA after receiving epoetin zeta subcutaneously.

Follow-up (12Aug2016): This is a follow-up report regarding subject 1160032. Immunogenicity testing results indicated antidrug antibody positive (titer=16), neutralizing antibody negative.

Follow-up (30Aug2016): This is a follow-up report received from Italian Health Authority, Regulatory Authority report number 314141. The Regional Centre for Pharmacovigilance stated that, according to Naranjo Algorithm, there was a possible relationship between the events and the drug.

Follow-up (10Jul2017): This is a follow-up report combining information from duplicate reports 2876300 and 2017150578. The current and all subsequent follow-up information will be reported under manufacturer report number 2876300. The new information reported from a contactable physician based on information received by Pfizer from Alvogen, local license partner for epoetin zeta (RETACRIT), includes:
A patient experienced pure red cell aplasia (PRCA) with the use of epoetin zeta (RETACRIT). The physician saw this title of the article on the web page of the company and reported this to an Alvogen sales representative. The title was "First case of pure red cell aplasia caused by biosimilar (epoetin zeta)".

Follow-up (23Nov2017): This is a follow-report from the site: the patient recovered from the events on 28Apr2016.

Case Comment: Overall case causality: Related Potential efficacy issue and sequela, but consider also administrative technique, error in dosing, drug storage, reported risk factors and patient-specific considerations, if any. Batch record review and retain

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

evaluation not done - no lot number. PRCA is related with the positive antibody testing result. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	MAY-2015	Anti-erythropoietin antibody		
2	29-MAY-2015	Anti-erythropoietin antibody	1: 81,920 titer: Positive	
3	17-JUN-2015	Anti-erythropoietin antibody	1: 40,960 titer: Positive	
4	03-JUL-2015	Anti-erythropoietin antibody	1: 40,960 titer: Positive	
5	MAY-2015	Antibody test	positive	
6	MAY-2015	Antinuclear antibody	normal	
7		Biopsy bone marrow	CD34 blasts revealed 20% cellular, reticulum thick	
8	APR-2015	Biopsy bone marrow	severe hypoplasia of the erythroid line	
9		Blood creatinine	3.7 mg/dl	1.1 0.4
10		Blood creatinine	3.1 mg/dl	1.1 0.4
11		Blood creatinine	3.1	1.1 0.4
12	01-DEC-2014	Blood creatinine	3.7 mg/dl	1.1 0.4
13	21-FEB-2015	Blood creatinine	3.7 mg/dl	1.1 0.4
14	25-FEB-2015	Blood creatinine	3.5 mg/dl	1.1 0.4
15	25-MAR-2015	Blood creatinine	3.85 mg/dl	1.1 0.4
16	09-APR-2015	Blood creatinine	3.7 mg/dl	
17	FEB-2016	Blood creatinine	3.9 mg/dl	
18	25-FEB-2015	Blood iron	2.27 ug/ml	
19	09-APR-2015	Blood iron	2.18 ug/ml	
20	25-FEB-2015	Blood parathyroid hormone	not applicable	
21	09-APR-2015	Blood parathyroid hormone	155 pg/ml	
22	FEB-2015	Bronchoscopy	unremarkable findings	
23	09-MAR-2015	Bronchoscopy	No lesions detectable within explorable areas	
24	09-APR-2015	C-reactive protein	0.3 mg/dl	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
25	FEB-2015	Colonoscopy	diverticulosis	
26	13-APR-2015	Colonoscopy	Csigmoid with lumen deformed by widespread diverti	
27	APR-2015	Colonoscopy	diverticulosis confirmed	
28	FEB-2015	Computerised tomogram	unremarkable finding	
29		Computerised tomogram thorax	Pleural isssues to the right	
30	05-MAR-2015	Computerised tomogram thorax	Cavitary formation of 5 cm maximum diameter	
31	DEC-2014	Culture stool	occult blood detected	
32	MAY-2015	DNA antibody	normal	
33		Echocardiogram	Moderate mitral regurgitation	
34	25-FEB-2015	Electrocardiogram	Sinus bradycardia	
35	09-APR-2015	Electrocardiogram	Sinus rhythm and RAV grade 1	
36		Endoscopy	Negative	
37	FEB-2015	Endoscopy	unremarkable findings	
38		Haematocrit	27.4	
39		Haematocrit	27.4	
40		Haematocrit	21	
41		Haematocrit	26.5	47 37
42	25-FEB-2015	Haematocrit	31 %	47 37
43	25-MAR-2015	Haematocrit	22.6 %	47 37
44	08-APR-2015	Haematocrit	17.6 %	47 37
45	21-APR-2015	Haematocrit	28.2 %	47 37
46	30-APR-2015	Haematocrit	24.7 %	47 37
47	12-MAY-2015	Haematocrit	20.3 %	47 37
48	18-MAY-2015	Haematocrit	18.6 %	47 37
49		Haemoglobin	9 g/dl	
50		Haemoglobin	9.6 g/dl	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
51		Haemoglobin	9.3 g/dl	16 12
52		Haemoglobin	7.3 g/dl	16 12
53		Haemoglobin	10 g/dl	
54	JUN-2014	Haemoglobin	9.7 g/dl	
55	01-DEC-2014	Haemoglobin	10.2 g/dl	16 12
56	21-FEB-2015	Haemoglobin	3.9 g/dl	16 12
57	25-FEB-2015	Haemoglobin	3.9 g/dl	
58	25-FEB-2015	Haemoglobin	10.6-9.3 g/dl	16 12
59	25-FEB-2015	Haemoglobin	9.3 post transfusion g/dl	
60	25-MAR-2015	Haemoglobin	8.1 g/dl	16 12
61	25-MAR-2015	Haemoglobin	8 g/dl	16 12
62	08-APR-2015	Haemoglobin	6.2 g/dl	16 12
63	09-APR-2015	Haemoglobin	7.3 post transfusion g/dl	16 12
64	09-APR-2015	Haemoglobin	6.2 g/dl	16 12
65	21-APR-2015	Haemoglobin	9.7 g/dl	16 12
66	30-APR-2015	Haemoglobin	8.5 g/dl	16 12
67	30-APR-2015	Haemoglobin	8.5 g/dl	16 12
68	12-MAY-2015	Haemoglobin	7.1 g/dl	16 12
69	18-MAY-2015	Haemoglobin	6.4 g/dl	16 12
70	FEB-2016	Haemoglobin	11.5 g/dl	
71	MAY-2015	Hepatitis B antibody	normal	
72	MAY-2015	Hepatitis B antibody	not detected	
73		Histology	Gastrooesophageal junction	
74	25-MAR-2015	Mean cell haemoglobin	80.1	99 81
75	25-MAR-2015	Mean cell haemoglobin	35.8 g/dl	35 31
76	08-APR-2015	Mean cell haemoglobin	80.7	99 81

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
77	08-APR-2015	Mean cell haemoglobin	35.2 g/dl	35 31
78	21-APR-2015	Mean cell haemoglobin	34.4 g/dl	35 31
79	21-APR-2015	Mean cell haemoglobin	83.9	99 81
80	30-APR-2015	Mean cell haemoglobin	34.4 g/dl	35 31
81	30-APR-2015	Mean cell haemoglobin	83.2	99 81
82	12-MAY-2015	Mean cell haemoglobin	82.2	99 81
83	12-MAY-2015	Mean cell haemoglobin	35 g/dl	35 31
84	18-MAY-2015	Mean cell haemoglobin	82.7	99 81
85	18-MAY-2015	Mean cell haemoglobin	34.4 g/dl	35 31
86		Mean cell volume	82.5	
87		Oesophagogastroscopy	Not reported	
88	25-FEB-2015	Platelet count	136000	
89	09-APR-2015	Platelet count	137000	
90	25-MAR-2015	Red blood cell count	2.82 x10 6/mm3	5.4 4.2
91	08-APR-2015	Red blood cell count	2.18 x10 6/mm3	5.4 4.2
92	21-APR-2015	Red blood cell count	3.36 x10 6/mm3	5.4 4.2
93	30-APR-2015	Red blood cell count	2.97 x10 6/mm3	5.4 4.2
94	12-MAY-2015	Red blood cell count	2.47 x10 6/mm3	5.4 4.2
95	18-MAY-2015	Red blood cell count	2.25 x10 6/mm3	5.4 4.2
96	25-MAR-2015	Red cell distribution width	14 %	14.5 11.5
97	08-APR-2015	Red cell distribution width	14.3 %	14.5 11.5
98	21-APR-2015	Red cell distribution width	13.6 %	14.5 11.5
99	30-APR-2015	Red cell distribution width	13.5 %	14.5 11.5
100	12-MAY-2015	Red cell distribution width	13.4 %	14.5 11.5
101	18-MAY-2015	Red cell distribution width	13.6 %	14.5 11.5
102		Reticulocyte count	0.1 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
103	09-APR-2015	Reticulocyte count	0.1 (2500 ul) %	
104	25-FEB-2015	Serum ferritin	268 ng/ml	
105	09-APR-2015	Serum ferritin	512 ng/ml	
106	JUN-2014	Spinal X-ray	unknown	
107	25-FEB-2015	Transferrin	201 mg/dl	
108	25-FEB-2015	Transferrin saturation	80.5 postr transfusion %	
109	09-APR-2015	Transferrin saturation	82.2 post transfusion %	
110	01-DEC-2014	Ultrasound abdomen	Within normal, right kidney with reduced cortex.	
111	APR-2015	Ultrasound abdomen	unremarkable for possible causes of anaemia	
112	15-APR-2015	Ultrasound abdomen	Hepatic portal vein within limits	
113	25-FEB-2015	White blood cell count	6850 /mm3	
114	09-APR-2015	White blood cell count	8680 /mm3	
115	JUN-2014	X-ray of pelvis and hip	unknown	
116	10-APR-2015	X-ray of pelvis and hip	Right coxarthrosis with coarse subchondral cysts	
117	10-APR-2015	X-ray of pelvis and hip	Vascular calcification	

13. Relevant Tests

Abd US: within normal, R kidney w/reduced cortex
Heart echo: systolic function conserved w/mod mitral regurg
CXR: pleural issues to R to be investigated further
Bone marrow Bx: 20% cellular, reticulum thickened, inc colorable deposits, lymphocytes 8% insterstitial and in small B and T aggregates, 5% polytipycal plasma cells markedly hypoplasic erythroid series, hyperplasia of megacariocyte and granulocyte line w/evidence of eosinophils series and CD34 blasts less than 5%.
Chest CT (05Mar2015): cavitary formation of around 5 cm max diameter w/walls w/irregular thickening assoc w/solid satellite nodules less than 1 cm tending to converge in subpleural region of posterior basal segment of LLL
ECG (25Feb2015): sinus bradycardia, T-wave negative/biphasic in lower ranges
Pancolonoscopy (13Apr2015): sigmoid w/lumen deformed by widespread diverticulosis and perivisceral inflammation, colon affected by hernia following L nephrectomy
Ferritin (25Feb2015): 268 ng/dL
Abd US (15Apr2015): liver dimensions w/in limits w/reg margins, surface, profiles and structure, affected by focal lesions; cholecystolithiasis, expanded in spite of recent meal, w/reg walls; at infundibular and first biliary duct level, thickening of the walls and endoluminal material not visible to US (biliary sludge); broad bile duct up to pancreas w/out obstructing endo or extra luminal images; hepatic portal vein w/in limits; suprahepatic veins reg; non-visible
Bone marrow Bx (Apr2015) severe hypoplasia of the erythroid line, CD34 blasts less than 5%, w/hyperplasia of megakaryocytic and granulocytic lines
Immunogenicity: indicates antidrug antibody pos (titer=16), neutralizing antibody neg

Mfr. Control Number: 2876300

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S017S4; Exp.Dt. 01-NOV-2016}; Regimen #1	100 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S033X4; Exp.Dt. 01-NOV-2016}; Regimen #2	100 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4T051U4; Exp.Dt. 01-DEC-2016}; Regimen #3	100 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4V067V4; Exp.Dt. 01-FEB-2017}; Regimen #4	100 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #5	4000 IU, 2x/week; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	JUN-2014 / FEB-2015; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #6	4000 IU, 3x/day; Subcutaneous	Renal anaemia (Nephrogenic anaemia) severe hip arthrosis (Osteoarthritis)	FEB-2015 / MAY-2015; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) FOLIC ACID (FOLIC ACID) Tablet ; Unknown

#8) PIPERACILLIN/TAZOBACTAM (PIPERACILLIN SODIUM, TAZOBACTAM SODIUM) ; Unknown

#9) SIMVASTATIN (SIMVASTATIN) Tablet ; Unknown

#10) SODIUM BICARBONATE (SODIUM BICARBONATE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Colonic diverticulosis (Diverticulum intestinal);
Unknown to Ongoing	Relevant Med History	Hiatal hernia (Hiatus hernia);
2006 to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Nephrolithiasis (Nephrolithiasis);
Unknown to Ongoing	Relevant Med History	Lower urinary tract infection (Urinary tract infection);
Unknown to Ongoing	Relevant Med History	Mitral regurgitation (Mitral valve incompetence);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Anemia (Anaemia);
1990 to Unknown	Relevant Med History	Acute hepatitis B (Acute hepatitis B);
1990 to Unknown	Relevant Med History	Blood transfusion (Transfusion);
1991 to Unknown	Relevant Med History	Extracorporeal shock wave lithotripsy (Lithotripsy);
Unknown	Relevant Med History	Pregnancy normal (Pregnancy);
JUN-2014 to Unknown	Relevant Med History	Radiotherapy (Radiotherapy);
JUN-2014 to Unknown	Relevant Med History	Gonalgia (Arthralgia);
JUN-2014 to Unknown	Relevant Med History	Coxalgia (Arthralgia);
1990 to Unknown	Relevant Med History	Sepsis (Sepsis);
1990 to Unknown	Relevant Med History	Urolithiasis (Calculus urinary);
2007 to Unknown	Relevant Med History	STEMI (Acute myocardial infarction);
1991 to Unknown	Relevant Med History	Renal calculus removal (Renal stone removal);
Unknown	Relevant Med History	Renal surgery (Renal surgery);
2007 to Unknown	Relevant Med History Risk Factor	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);
Unknown	Relevant Med History Acute pyelonephritis	Pyelonephritis acute (Pyelonephritis acute);
1995 to Unknown	Relevant Med History for obstructive nephrolithiasis	Nephrostomy (Nephrostomy);
2007 to 2014	Relevant Med History reaching stage IV-V CKD	Function kidney decreased (Renal impairment);
1990 to Unknown	Relevant Med History	Nephrectomy (Nephrectomy);
1991 to Unknown	Relevant Med History received extracorporeal shock wave lithotripsy	Nephrolithiasis (Nephrolithiasis);
1991 to Unknown	Relevant Med History	Extracorporeal shock wave lithotripsy (Lithotripsy);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	GERMANY	06	JUL	1928	86 Years	Male	74.00 kg	07	APR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11, regarding subject GE115|0124.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 22-JUL-2014 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACTRAPHANE (INSULIN HUMAN, INSULIN HUMAN INJECTION,
#2) ADENURIC (FEBUXOSTAT) ; Unknown
#3) AMLODIPINE (AMLODIPINE) ; Unknown
#4) ASS (ACETYLSALICYLIC ACID) ; Unknown
#5) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown
#6) MOXONIDIN (MOXONIDINE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
07-APR-2015 to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia)
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus)
	insulin-dependent	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017095459

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
29-JUN-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 86-year-old Caucasian male subject started taking epoetin zeta 5000 (units unspecified) subcutaneously weekly, on 22Jul2014 for the study indication renal anemia. Medical history included ischemic heart disease since 07Apr2015, type 2 diabetes mellitus insulin-dependent, arterial hypertension, all ongoing, and chronic renal insufficiency stage 4-5 and coronary two vessel disease. Concomitant medications included insulin human/ insulin human injection/ isophane (ACTRAPHANE) 50 (units unspecified), febuxostat (ADENURIC) 80 mg, amlodipine 5 mg twice a day, acetylsalicylic acid (ASS) 100 mg once a day, clopidogrel bisulfate (PLAVIX) 75 mg once a day, moxonidine 0.3 mg twice a day, ramipril (DELIX) 5 mg twice a day, tamsulosin 0.4 mg once a day, torasemide (TOREM) 50 mg twice a day, and cefamandole nafate (TEVACIDOL) 0.25 mg once a day since 22Jul2014. On 07Apr2015, the subject experienced a Non-ST-segment elevation myocardial infarction (NSTEMI). The subject was hospitalized, on the same date, due to retrosternal stinging and feeling of pressure combined with vomiting. The subject had a cardiac catheter examination on 07Apr2015 that showed a coronary two-vessel disease. A clinical physical examination during admission showed a reduced general state of health. The subject had a clear consciousness, dry skin, dry mucous membrane, lung: fine rales on the left; heart: rhythmical, no pathological heart murmurs, abdomen: no muscular defense, regular peristaltic sounds, no pressure pain, no melena, no renal bed percussion pain, no peripheral edemas, amputation of the left foot, no lymph node enlargement; neurological examination findings: unobtrusive, especially no meningism. Additional test data included an coronary angiography that showed moderately severe coronary sclerosis, ramus interventricularis anterior (RIVA): moderately severe coronary sclerosis, 40% lumen reduction of the proximal ramus interventricularis anterior, 90& stenosis of the ramus intermedius (American heart association (AHA) type C2, length > 25), ramus circumflexus: severe coronary sclerosis, 95% stenosis of the medial ramus circumflexus, right coronary artery severe coronary stenosis, 50% stenosis of the medial right coronary artery on 07Apr2015, cholesterol 217 mg/dl on 09Apr2015, creatine phosphokinase 186.6 IU/l (normal high: 200 IU/l) on 07Apr2015, 363.4 IU/l on 08Apr2015 and 215.7 IU/l on 09Apr2015, creatine phosphokinase MB 59.4 IU/l (normal high: 24 IU/l) on 08Apr2015, creatinine 3.49 mg/dl on 07Apr2015, 2.98 mg/dl on 08Apr2015 and 3.57 mg/dl on 09Apr2015, glucose 100 mg/dl on 09Apr2015, glucose in serum 192.2 mg/dl (70 to 105 mg/dl) on 07Apr2015 and 178.6 mg/dl on 09Apr2015, blood sugar 294 mg/dl on 08Apr2015, 350 mg/dl on 08Apr2015, 386 mg/dl on 08Apr2015 and 165 mg/dl on 09Apr2015, lactate dehydrogenase (LDH) 311 IU/l on 09Apr2015,cHBc POCTv test of 10.9 g/dl (11.7 to 17.4 g/dl),a Glu POCTv 191 mg/dl (70 to 100 mg/dl) and 253 mg/dl, an Hkt POCTv test of 32% (35 to 51%) on 07Apr2015 and 33% on 07Apr2015, a pCO2 POCTv test of 41 mmHG (42 to 55 mmHg), a TCO2 POCTv of 28.6 mmol/l (22 to 26 mmol/l) on 07Apr2015 and 26.1 mmol/l on 07Apr2015, a SCO2 POCTv of 76% (90 to 98%) on 07Apr2015, urea 248.8 mg/dl (8 to 55 mg/dl) on 07Apr2015, 203.2 mg/dl on 08Apr2015 and 212.1 mg/dl on 09Apr2015, C-reactive protein (CRP) 5.84 mg/l (normal high 5.00 mg/l) on 07Apr2015, glomerular filtration rate (GFR) 15 ml/min on 07Apr2015, GFR n. CKD-EPI 15.0 (normal low of 9) on 07Apr2015, 18.1 on 08Apr2015 and 14.1 on 09Apr2015, hemoglobin A1C (HbA1C) 7.04% on 07Apr2015, hematocrit 31.9% (46 to 54%) on 07Apr2015, 30.3% on 08Apr2015 and 32% on 09Apr2015, hemoglobin 10.9 g/dl (12.0 to 16.0 g/dl) on 22Jul2014, 10.8 g/dl on 07Apr2015, 10.1 g/dl on 08Apr2015 and 10.5 g/dl on 09Apr2015, mean cell hemoglobin concentration (MCHC) 32.8 g/dl (33 to 35 g/dl) on 09Apr2015, thrombocytes 145 x10 3/mm3 (150 to 450 x10 3/mm3) on 08Apr2015 and 148 x10 3/mm3 on 09Apr2015, pro-Calcitonin, quan KS-PCTQ 0.21 ng/ml (normal high of 0.1 ng/ml), total protein 5.7 g/dl (6.0 to 8.3 g/dl) on 08Apr2015, erythrocytes 3.4 x10 6/mm3 (3.5 to 6.0 x10 6/mm3) on 07Apr2015, 3.19 x10 6/mm3 on 08Apr2015 and 3.31 x10 6/mm3 on 09Apr2015, erythrocytes 10 /mm3 on 08Apr2015 and 10 /mm3 on 09Apr2015, troponin 0.135 ng/ml (normal high: 0.228 ng/ml) and 12.117 ng/ml on 08Apr2015, a resting electrocardiogram that showed vertical heart position, sinus rhythm 90/min, ST-reduction II,III, augmented voltage left foot, V4-V6 Thorax on 07Apr2015, a thorax (chest) x-ray while sitting anterior-posterior that showed right diaphragm definable, costodiaphragmatic angle not completely exposed, left diaphragm not demarcated due to heart shadow overlap, heart in rectangular diameter clearly enlarged, calcification in the aortic knob; no central or peripheral pulmonary hypervolemia; no enlarged, typical, pneumonic infiltrations on 07Apr2015. The subject was treated with a percutaneous coronary intervention (PCI) stenosis of ramus circumflexus with stent implantation. The subject underwent a PCI of a 95% stenosis of the medial ramus circumflexus to 0% via biomatrix stent-implantation and of a 90% stenosis of the ramus circumflexus via drug eluting stent (DES)-implantation and bare metal stent (x2). The subject was also given fluids due to progressive renal insufficiency. After the examination, the subject was transferred to the monitoring station. The course was uncomplicated and the subject was moved to a normal station on the next day. The complaints declined significantly. As for the known renal insufficiency stage 5, the subject received infusions whereby the retention values remained stable. A periodic control of the renal values were recommended. With regard to the radiologic aspects, there were no indications of a left cardiac decompensation or a bronchopneumonic formation of lesions. It was also recommend to have a specific follow-up concerning the drug eluting stent implantation for at least 9 months with acetylsalicylic acid (ASS) and clopidogrel in combination. When the values for blood glucose increase, a therapy with insulin was necessary. Periodic blood pressure monitoring and possibly further adjustment of the antihypertensive therapy was requested. All concomitant medications were recommended to be continued, whereby ASS was to be given for a lifetime and clopidogrel (PLAVIX) was to be continued for 9 months. No action was taken with epoetin zeta in response to the event. On 10Apr2015, the subject was discharged from the hospital, in an improved condition, for outpatient follow-up care. On 10Apr2015, the subject recovered from the event. The investigator stated that there was not a reasonable possibility that the event, NSTEMI, was related to epoetin zeta.

Follow-up (29Jun2017): Updates concomitant medication details, action taken with study drug.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, Non-ST-segment elevation myocardial infarction, was related to the study drug, placebo, concomitant drugs or associated with a clinical trial procedure. Underlying ischemic heart disease, coronary two vessel disease, type 2 diabetes mellitus insulin-dependent, and arterial hypertension may be regarded as the most likely explanations for the reported event.

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-APR-2015	Angiogram	Moderately severe coronary sclerosis	
2	09-APR-2015	Blood cholesterol	217 mg/dl	200
3	07-APR-2015	Blood creatine phosphokinase	186.6 IU/l	200
4	08-APR-2015	Blood creatine phosphokinase	363.4 IU/l	200
5	09-APR-2015	Blood creatine phosphokinase	215.7 IU/l	200
6	08-APR-2015	Blood creatine phosphokinase MB	59.4 IU/l	24
7	07-APR-2015	Blood creatinine	3.49 mg/dl	1.25 0.72
8	08-APR-2015	Blood creatinine	2.98 mg/dl	1.25 0.72
9	09-APR-2015	Blood creatinine	3.57 mg/dl	1.25 0.72
10	07-APR-2015	Blood glucose	192.2 mg/dl	105 70
11	09-APR-2015	Blood glucose	100 mg/dl	
12	09-APR-2015	Blood glucose	178.6 mg/dl	105 70
13	08-APR-2015	Blood glucose abnormal	386 mg/dl	100 60
14	08-APR-2015	Blood glucose abnormal	294 mg/dl	100 60
15	08-APR-2015	Blood glucose abnormal	350 mg/dl	100 60
16	09-APR-2015	Blood glucose abnormal	165 mg/dl	100 60
17	09-APR-2015	Blood lactate dehydrogenase	311 IU/l	220
18	07-APR-2015	Blood test	41 mmHg	55 42
19	07-APR-2015	Blood test	10.9 g/dl	17.4 11.7
20	07-APR-2015	Blood test	26.1 mmol/l	26 22
21	07-APR-2015	Blood test	28.6 mmol/l	26 22
22	07-APR-2015	Blood test	33 %	51 35
23	07-APR-2015	Blood test	32 %	51 35
24	07-APR-2015	Blood test	253 mg/dl	100 70
25	07-APR-2015	Blood test	191 mg/dl	100 70
26	07-APR-2015	Blood test abnormal	76 %	98 90
27	07-APR-2015	Blood urea	248.8 mg/dl	55 8

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
28	08-APR-2015	Blood urea	203.2 mg/dl	55 8
29	09-APR-2015	Blood urea	212.1 mg/dl	55 8
30	07-APR-2015	C-reactive protein increased	5.84 mg/l	5.00
31	09-APR-2015	C-reactive protein increased	8.04 mg/l	5.00
32	07-APR-2015	Chest X-ray	No central or peripheral pulmonary hypervolemia	
33	07-APR-2015	Electrocardiogram	vertical heart position, sinus rhythm 90/min, ST-r	
34	07-APR-2015	Glomerular filtration rate	15 ml/min	
35	07-APR-2015	Glomerular filtration rate	15.0	9
36	08-APR-2015	Glomerular filtration rate	18.1	9
37	09-APR-2015	Glomerular filtration rate	14.1	9
38	07-APR-2015	Glycosylated haemoglobin	7.04 %	
39	07-APR-2015	Haematocrit	31.9 %	54 36
40	08-APR-2015	Haematocrit	30.3 %	54 36
41	09-APR-2015	Haematocrit	32 %	54 36
42	22-JUL-2014	Haemoglobin	10.9 g/dl	16.0 12.0
43	07-APR-2015	Haemoglobin	10.8 g/dl	16.0 12.0
44	08-APR-2015	Haemoglobin	10.1 g/dl	16.0 12.0
45	09-APR-2015	Haemoglobin	10.5 g/dl	16.0 12.0
46	09-APR-2015	Mean cell haemoglobin concentration	32.8 g/dl	35 33
47	07-APR-2015	Physical examination	Coronary two-vessel disease	
48	07-APR-2015	Physical examination	Reduced general state of health	
49	08-APR-2015	Platelet disorder	145 x10 3/mm3	450 150
50	09-APR-2015	Platelet disorder	148 x10 3/mm3	450 150
51	08-APR-2015	Procalcitonin	0.21 ng/ml	0.1
52	08-APR-2015	Protein total decreased	5.7 g/dl	8.3 6.0
53	07-APR-2015	Red blood cell abnormality	3.4 x10 6/mm3	6.0

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				3.5
54	08-APR-2015	Red blood cell abnormality	10 /mm3	0
55	08-APR-2015	Red blood cell abnormality	3.19 x10 6/mm3	6.0 3.5
56	09-APR-2015	Red blood cell abnormality	3.31 x10 6/mm3	6.0 3.5
57	09-APR-2015	Red blood cell abnormality	10 /mm3	0
58	07-APR-2015	Troponin	0.135 ng/ml	0.228
59	08-APR-2015	Troponin	12.117 ng/ml	0.228

13. Relevant Tests

Resting electrocardiogram (07Apr2015): vertical heart position, sinus rhythm 90/min, ST-reduction II,III, augmented voltage left foot, V4-V6
Thorax (chest X-ray) while sitting anterior--posterior (07Apr2015): Right diaphragm definable, costodiaphragmatic angle not completely exposed, left diaphragm not demarcated due to heart shadow overlap, heart in rectangular diameter clearly enlarged, calcification in the aortic knob. No central or peripheral pulmonary hypervolemia. No enlarged, typical, pneumonic infiltrations.
Coronary angiography (07Apr2015): Main stem: Moderately severe coronary sclerosis, ramus interventricularis anterior (RIVA): moderately severe coronary sclerosis, 40% lumen reduction of the proximal ramus interventricularis anterior, 90& stenosis of the ramus intermedius (American heart association [AHA] type C2, length > 25), ramus circumflexus: severe coronary sclerosis, 95% stenosis of the medial ramus circumflexus, right coronary artery severe coronary stenosis, 50% stenosis of the medial right coronary artery

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) ACTRAPHANE (INSULIN HUMAN, INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown

#7) DELIX (RAMIPRIL) ; Unknown

#8) TAMSULOSIN (TAMSULOSIN) ; Unknown

#9) TOREM (TORASEMIDE) ; Unknown

#10) TEVACIDOL (CEFAMANDOLE NAFATE) ; 22-JUL-2014 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension);
Unknown	Relevant Med History	Chronic renal insufficiency (Chronic kidney disease);
Unknown	Relevant Med History	Double vessel disease (Coronary artery disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	21	AUG	1940	74 Years	Female	60.00 kg	14	OCT	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Thromboembolic events [Embolism]
Stroke [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

Thromboembolic event. Epoetin zeta.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 23-NOV-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) FISIOTENS (MOXONIDINE) ; Unknown
#2) LASIX (FUROSEMIDE) ; Unknown
#3) ADALAT (NIFEDIPINE) ; Unknown
#4) RANEXA (RANOLAZINE) ; Unknown
#5) LANTUS (INSULIN GLARGINE) ; Unknown
#6) LEXOTANIL (BROMAZEPAM) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
21-JUN-2010 to Ongoing	Relevant Med History	Renal failure (Renal failure)
Unknown to Ongoing	Relevant Med History	Renovascular hypertension (Renovascular hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2880827

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-FEB-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Serious Hospira sponsored study report from Greece received from an investigator (ref: Gr-051-0041) which refers to a female Caucasian patient (dry weight: 60 kg, height: 170 cm; age not reported).
The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history included renovascular which led to the diagnosis of renal failure on 21-Jun-2010. The patient had not been treated with an Erythropoiesis Stimulating Agent (ESA) before treatment with Retacrit and had not received Retacrit previously. The patient was not on dialysis. On 23- Nov-2013, the patient started to receive treatment with epoetin zeta (Retacrit, 166.7 IU/kg/week, 1 dosage per week, subcutaneous; lot number not reported) for renal anaemia. On an unknown date, on the 12-month visit point, the patient developed thrombembolic events. Laboratory or diagnostic tests, treatment, action taken with the suspect drug in response to the event and outcome were not provided. The reporter's opinion of causality between the event and epoetin zeta was not provided. Risk factors included coronary heart disease, myocardial infarction, atrial fibrillation, peripheral artery disease, hypertension, diabetes type 2, heart failure NYHA stage II and smoking. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): lot number, date of expiry, and previous exposure of patient to other biosimilars.

Follow-up (19Jan2018): New information received from a contactable physician from a Non-Interventional study report for Protocol EPOE-09-11 (C1111006), regarding subject GR0510041.

This is updated case information, regarding patient GR0510041 case: 2880827. The patient was hospitalized from 14Oct2014 until 23Oct2014, due to stroke/thromboembolic event. This event is not related to study drug.

Amendment: this report is being submitted to add the reporter causality (unrelated)

Follow-up (01Feb2018). This is a follow-up report from the investigator. The mean dose of Epoetin Zeta applied within the period of 3 months prior to the event was 10000 per week. The patient was not exposed at any time to any other erythropoietin stimulating agent (ESA). Relevant medical history included ongoing smoking, ongoing vascular anomalies, ongoing ischaemic heart disease, diabetes mellitus from 1987 and ongoing, hypertension from 1989 and ongoing, and chronic gastrointestinal disease. Concomitant medications included moxonidine (FISIOTENS) at 0.4 (no units provided), 1x/day for hypertension, furosemide (LASIX) at 40 (no units provided), 1x/day for hypertension, nipedipine (ADALAT) at 60 (no units provided), 1x/day for hypertension, ranolazine (RANEXA) at an unknown dose, 1x/day for heart failure and atrial fibrillation, insulin glargine (LANTUS) at an unknown dose, 1x/day for diabetes and bromazepam (LEXOTANIL) at 1.5 (no units provide), 1x/day for a non reported indication. On an unspecified date the patient underwent laboratory examination that showed, haemoglobin 10.4 g/dl and 10.7 g/dl, haematocrit 32.4 %, reticulocytes 297000, red blood cells 3.17 M/microliter and CRP 9.7 mg/dl. The investigator considered that the events were life-threatening.

Follow-up attempts completed. No further information is expected.

Amendment: this report is being submitted to add patient's age at onset.

Amendment: This report is being submitted to clarify that the patient's age at onset of the event was determined to be 74 years old.

Case Comment: The Company considers there is a reasonable possibility that the reported events Thromboembolic events and Stroke are related to EPOETIN ZETA based on the temporal association and the known safety profile of the product. Patient's medical history of coronary heart disease, myocardial infarction, atiral fibrillation, peripheral artery disease, hypertension, diabetes type 2, heart failure NYHA stage II and smoking may have also played a contributory role.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		C-reactive protein	9.7 mg/dl	
2		Haematocrit	32.4 %	
3		Haemoglobin	10.4 g/dl	
4		Haemoglobin	10.7 g/dl	
5		Red blood cell count	3.17	
6		Reticulocyte count	297000	

Mfr. Control Number: 2880827

ADDITIONAL INFORMATION

13. Relevant Tests

Red blood cell (unknown): 3.17 M/microliter

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	10000 IU, weekly; 166.7 IU/kg weekly; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	23-NOV-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
1987 to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
1989 to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Smoker (Tobacco user);
Unknown to Ongoing	Relevant Med History	Vascular disorder NOS (Angiopathy);
Unknown to Ongoing	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History	Gastrointestinal disorder NOS (Gastrointestinal disorder);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	20	SEP	1942	72 Years	Male	74.00 kg	08	MAY	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cerebral hemorrhage [Cerebral haemorrhage]
Kidney failure (uremia) [Renal failure]
Kidney failure(uremia) [Azotaemia]

Case Description: Fatal kidney failure (uremia) and cerebral hemorrhage. Epoetin zeta. Hospira sponsored clinical study report received from an Investigator (reference: Sw-005-0031), which refers to a patient. The patient was enrolled in a Hospirasponsored
Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 03-DEC-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 54 IU/kg/week, 0.5dosage/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low HB (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 28-NOV-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) BEHEPAN /00056201/ (CYANOCOBALAMIN) Tablet ; 17-APR-2013 / Unknown
#2) BUDENOFALK (BUDESONIDE) ; 27-MAY-2015 / Unknown
#3) CARVEDILOL HEXAL (CARVEDILOL) Tablet ; 14-MAR-2013 / Unknown
#4) COSMOFER (IRON DEXTRAN) Solution for injection ; 19-AUG-2014 / Unknown
#5) DIMOR (LOPERAMIDE HYDROCHLORIDE) Tablet ; 18-SEP-2014 / Unknown
#6) DIVISUN (COLECALCIFEROL) Tablet ; 14-MAY-2015 / Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Crohn's (Crohn's disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2893017

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-SEP-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Patient's medical history included ischemic heart disease, chronic gastrointestinal disease (Crohn), intermittent diarrhea, nystagmus and diabetic nephropathy which led to renal failure diagnosed on 23-Nov-2011. The patient was on hemodialysis 3x/week which started on 31-Jan-2014, also reported as 03-Mar-2014. The patient was not treated with an ESA before treatment with Retacrit. The patient had no earlier exposure to other biosimilars. Concomitant medications included Laxido Orange powder for oral solution, Behepan film-coated tablets 1 mg, carvedilol Hexal tablets 25 mg, Insuman Basal Solostar injection fluid, suspension in pre-filled injection pens 100 IU/ml, Glytrin sublingual spray 0.4 mg /dose, warfarin, Dimor film-coated tablets 2 mg, Budenofalk Enterogranulate 9 mg, Divisun tablet 800 IU, Oralovite tablets, simvastatin KRKA film-coated tablet 10 mg, Remeron-S, Heminevrin oral solution 50 mg/ml, sodium bicarbonate prescription tablet 1 g, NovoRapid Penfill injection fluid, 100 U/ml solution in cylinder ampoules, Innohep injection fluid, solution, pre-filled syringe and Innohep injection fluid, 10000 anti-Xa IU/ml solution; Cosmofer injection fluid, 50 mg/ml solution, Furix injection fluid, 10 mg/ml solution, Trandate injection fluid, 5 mg/ml solution, Ketogan Novum injection fluid 5 mg/ml solution and paracetamol B. Braun infusion fluid, 10 mg/ml solution. On 28-Nov-2012, the patient started treatment with epoetin zeta (Retacrit; 54 IU/kg/week, 0.5 dosage/week, frequency also reported as once a week, subcutaneous; lot number and presentation unknown) for low HB. Date informed consent signed was on 07-May-2014. On 01-Apr-2015 at 10:00, the patient's B-hemoglobin was at 116 g/L (normal range: 134-170), B-EVF at 0.35 (unit of measurement not reported, normal range: 0.40-0.50), B-erythrocytes at 3.8 x 10^12/L (normal range: 4.3-5.7) and B-thrombocytes at 277 x 10^9/L (normal range: 140-350). On 08-May-2015, the patient experienced cerebral hemorrhage described as hemiparesis. It was reported that the patient was admitted to a hospital on the same day, where patient also received the last dose prior to the event. On the same day at 23:25, CT of head was performed which showed approximately 2-cm large intracerebral bleeding in right thalamus with slight surrounding oedema and third ventricle slightly compressed. Primarily hypertonia-induced bleeding. Pronounced white matter changes seen bilaterally. Minor older infarcts in left cerebellar hemisphere and left occipital lobe. And also on the same day at 23:45, the patient's B-hemoglobin was at 135 g/L, B-EVF at 0.39, B-erythrocytes at 4.4 x 10^12/L, B-thrombocytes at 256 x 10^9/L, P-activated partial thromboplastin time at 33 s (normal range: 24-32) and P-PK-International Normalized Ratio (INR) at 1.7 (unit of measurement not reported, normal range: 0.8-1.2). On 25-May-2015 at 11:45, the patient's Bhemoglobin was at 107 g/L, B-EVF at 0.32, B-erythrocytes at 3.6 x 10^12/L, B-thrombocytes at 339 x 10^9/L. Treatment for the adverse event included Konakion, Ocplex, ASA (doses and routes of administration not reported), and discontinuation of warfarin. Action taken with the suspect drug was reported as none. The patient had not recovered from the event at the time of the report. On 16-Jun-2015, the patient was discharged from the hospital. On an unknown date, the patient experienced kidney failure (uremia) due to on his own request to end dialysis treatment on 16-Nov-2015. Treatment for the event of kidney failure (uremia) and action taken in response to the said event were not reported. On 03-Dec-2015, the patient died. Cause of death was kidney failure (uremia). It was not reported if an autopsy was performed. The reporter's causality assessment for the events of fatal kidney failure (uremia) and cerebral hemorrhage in relation to epoetin zeta was not related. It was reported that cerebral bleeding was due to anticoagulant. Risk factors included history of smoking until 1993 (ex-smoker), heart surgery (transfemoral, TAVI) on 18-Mar-2015; warfarin use and hypertension, coronary heart disease, hyperlipidemia, diabetes mellitus type 1 with no diabetic vascular complications, and stroke in 2001 and 2002. 08-Jun-2015: Additional information from the same reporter and English translation of the Swedish text were received. Presentation of Retacrit was not known. Action taken with Retacrit relative to the event was reported as none. It was reported that the patient had no earlier exposure to other biosimilars, and that cerebral bleeding was due to anticoagulant. Cerebral hemorrhage was described as hemiparesis (previously reflected as hemipares). Intermittent diarrhea and nystagmus were added as patient's medical history. CT of head was added as diagnostic procedure. Doses, routes of administration and therapy start dates of concomitant medications; and indications of Laxido orange powder, Insuman Basal Solostar, Behepan, carvedilol Hexal and Glytrin; and time for the laboratory tests were also provided. Start date of hemodialysis was also reported as 03-Mar-2014; while therapy start date of Retacrit was also reported as 28-Nov-2012. This information has been incorporated in the narrative and corresponding data fields. 25-Sep-2015: Additional information was received from the same reporter. Therapy start date of Retacrit was updated to 28-Nov-2012 (previously 14-Mar-2014). Patient's discharge date was provided. This information has been incorporated in the narrative and corresponding data fields. 22-Dec-2015: Additional information was received from the same reporter. Fatal kidney failure (uremia) was added as an adverse event. This information has been incorporated in the narrative and corresponding data fields. Data entry correction was also made to add ex-smoker in the narrative.

Case Comment: Overall case causality: Related While reporter causality and predisposing risk factors are noted, consider also contributory role of the suspect drug for this temporally related and labeled event. Follow-up: No change in assessment. Follow-up: Causality changed to not related as the stroke was noted to be a cerebral hemorrhage and due to the anticoagulant treatment. Follow-up: The added adverse event of fatal renal failure is also not related as this is a likely progression of patient's preexistent condition.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-MAY-2015	Activated partial thromboplastin time	33 seconds	32 24
2	08-MAY-2015	Computerised tomogram head	Pronounced white matter	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			changes seen bilaterally U	
3	08-MAY-2015	Computerised tomogram head	Approximately 2 cm large intracerebral bleeding U	
4	08-MAY-2015	Computerised tomogram head	Minor older infarct in left occipital lobe Unknown	
5	08-MAY-2015	Computerised tomogram head	Minor older infarct in left cerebellar hemisphere	
6	01-APR-2015	Haematocrit	0.35 Unknown	0.50 0.40
7	08-MAY-2015	Haematocrit	0.39 Unknown	0.50 0.40
8	25-MAY-2015	Haematocrit	0.32 Unknown	0.50 0.40
9	01-APR-2015	Haemoglobin	116 g/l	170 134
10	08-MAY-2015	Haemoglobin	135 g/l	170 134
11	25-MAY-2015	Haemoglobin	107 g/l	170 134
12	08-MAY-2015	International normalised ratio	1.7 Unknown	1.2 0.8
13	01-APR-2015	Platelet count	277 x10 9/l	350 140
14	08-MAY-2015	Platelet count	256 x10 9/l	350 140
15	25-MAY-2015	Platelet count	339 x10 9/l	350 140
16	01-APR-2015	Red blood cell count	3.8 x10 12/l	5.7 4.3
17	08-MAY-2015	Red blood cell count	4.4 x10 12/l	5.7 4.3
18	25-MAY-2015	Red blood cell count	3.6 x10 12/l	5.7 4.3

13. Relevant Tests

CT of head(08-May-2015) :- Approximately 2 cm large intracerebral bleeding Unknown
CT of head(08-May-2015) :- Minor older infarct in left cerebellar hemisphere Unknown
CT of head(08-May-2015) :- Pronounced white matter changes seen bilaterally Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) FURIX (FUROSEMIDE) Solution for injection ; 11-MAY-2015 / Unknown

#8) GLYTRIN (GLYCERYL TRINITRATE) ; 25-SEP-2014 / Unknown

#9) HEMINEVRIN /00027501/ (CLOMETHIAZOLE) Oral solution ; 24-MAY-2015 / 31-MAY-2015

#10) INNOHEP (TINZAPARIN SODIUM) Solution for injection in pre-filled syringe ; 07-FEB-2014 / Unknown

#11) INSUMAN BASAL (INSULIN HUMAN INJECTION, ISOPHANE) ; 14-MAR-2013 / Unknown

#12) KETOGAN NOVUM (KETOBEMIDONE HYDROCHLORIDE) Solution for injection ; 24-MAY-2015 / 29-MAY-2015

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#13) MOVICOL /08437601/ (MACROGOL, POTASSIUM CHLORIDE, SODIUM BICARBONATE) Oral solution ; 25-MAY-2015 / Unknown

#14) NOVORAPID (INSULIN ASPART) ; 19-MAY-2015 / 09-JUN-2015

#15) ORALOVITE (ASCORBIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) Tablet ; 28-AUG-2013 / Unknown

#16) PARACETAMOL B. BRAUN (PARACETAMOL) Solution for infusion ; 09-MAY-2015 / Unknown

#17) REMERON (MIRTAZAPINE) Tablet ; 28-MAY-2015 / Unknown

#18) SIMVASTATIN KRKA (SIMVASTATIN) Tablet ; 28-MAY-2015 / Unknown

#19) TRANDATE (LABETALOL HYDROCHLORIDE) Solution for injection ; 09-MAY-2015 / Unknown

#20) SODIUM BICARBONATE (SODIUM BICARBONATE) Tablet ; 06-NOV-2014 / Unknown

#21) WARFARIN (WARFARIN) ; 19-MAR-2015 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Patient's medical history included ischemic heart disease, chronic gastrointestinal disease (Crohn), intermittent diarrhea, nystagmus and diabetic nephropathy which led to renal failure diagnosed on 23-Nov-2011. The patient was on hemodialysis 3x/week which started on 31-Jan-2014. The patient was not treated with an ESA before treatment with Retacrit. The patient had no earlier exposure to other biosimilars. Risk factors included history of smoking until 1993 (ex-smoker), heart surgery (transfemoral, TAVI) on 18-Mar-2015, warfarin and hypertension, coronary heart disease, hyperlipidemia, diabetes mellitus type 1 with no diabetic vascular complications, and stroke in 2001 and 2002. Allergies and alcohol consumption were not reported. Race/Ethnicity: Caucasian On 03-Dec-2015, the patient died. Cause of death was kidney failure (uremia). It was not reported if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Diarrhea (Diarrhoea);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Nystagmus (Nystagmus);
Unknown to Ongoing	Relevant Med History 23-Nov-2011	Renal failure (Renal failure);
Unknown	Relevant Med History	Type I diabetes mellitus without mention of complication (Type 1 diabetes mellitus);
Unknown	Relevant Med History 18-Mar-2015	Open heart surgery (Cardiac operation);
Unknown	Relevant Med History Stopped on 1993	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History 2001 and 2002	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History 19-Mar-2015	Anticoagulant therapy (Anticoagulant therapy);
Unknown	Relevant Med History	Dialysis (Dialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	20	NOV	1945	69 Years	Male	74.00 kg	01	MAR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombosis of right ileac artery [Peripheral artery thrombosis]

Case Description: Thrombosis of right ileac artery. Epoetin zeta. Serious Hospira-sponsored clinical study report from Bulgaria received from an investigator (reference: Bg-004-0017), which refers to a 70-year-old Caucasian male patient (dry weight: 74 kg,
height: 170 cm). The patient was enrolled in a Hospira-sponosored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Medical history

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 40 IU/kg, Freq: 1 week; Interval: 1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 01-JUL-2013 / 23-MAR-2015	#1) 631 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSUMAN BASAL (INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown
#2) LORISTA (LOSARTAN POTASSIUM) ; Unknown
#3) THIOGAMMA (THIOCTIC ACID) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown Unknown to Ongoing	Relevant Med History	() Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2896188

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-JUN-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2896188

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

included diabetic nephropathy which led to renal failure diagnosed on 01 May 2013. The patient was not on dialysis. It was reported that the patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications included Insuman Basal (26 UI, once) for diabetes mellitus, Lorista (50 mg, once) for hypertension and Thiogamma (600 mg, once) for diabetic polyneuropathy (routes of administration not reported). On 01 Jul 2013, the patient started treatment with epoetin zeta (Retacrit; 40 IU/kg/week, subcutaneous; lot number reported as NA) for renal anaemia. Mean dose was 3000 UI weekly. Informed consent was signed on 27 Jan 2014. On an unknown date in March 2015, the patient experienced thrombosis of right ileac artery. The patient's haemoglobin was 9.9 g/dL. As treatment, the patient underwent an unspecified operation. He was hospitalized because of the adverse event (considered life-threatening by the investigator) from an unknown date in March 2015 to 24 Mar 2015. The patient received the last dose of Retacrit on 23 Mar 2015. The patient reportedly recovered from the event on 24 Mar 2015. The investigator's causality assessment between the event and Retacrit was not related. Risk factors included coronary heart disease, ischemic heart disease, peripheral arterial disease in May 2013, diabetes mellitus type 2 in 2004, hypertension in 2004 and heart failure NYHA stage II in 2004. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: lot number and date of expiry.

Case Comment: Overall case causality: Related A labeled event, but consider also other reported risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	9.9 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to renal failure diagnosed on 01 May 2013. The patient was not on dialysis. It was reported that the patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Risk factors included coronary heart disease, ischemic heart disease, peripheral arterial disease in May 2013, diabetes mellitus type 2 in 2004, hypertension in 2004 and heart failure NYHA stage II in 2004. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History Diagnosed on 01 May 2013	Renal failure (Renal failure);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor- in 2004	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History Risk Factor- in 2004	Heart failure NYHA class II (Cardiac failure chronic);
Unknown	Relevant Med History Risk Factor- in 2004	Hypertension (Hypertension);
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Risk Factor- May 2013	Peripheral arterial disease (Peripheral arterial occlusive disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	22	JUL	1937	77 Years	Male	79.80 kg	09	FEB	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: Lack of efficacy. Epoetin zeta. Serious Hospira-sponsored study report from Italy, received from an investigator (reference: It-116-0022), which refers to a 77-year-old Caucasian male patient (dry weight: 79kg, height: 175 cm). The
patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Medical history included diabetic nephropathy

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 27 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 12-JUN-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Arteriosclerotic cardiovascular disease (Arteriosclerosis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2899611

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-JUN-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

which led to renal failure diagnosed in 12-Oct-2004. The patient has been regularly monitored for moderate renal failure, secondary to diabetic nephropathy and cardiovascular disease, in a clinic since 2004. In May of that year, the patient developed anaemia and his renal function worsened. As a consequence, the patient was admitted to hospital. The patient was not on dialysis. Concomitant disease included arteriosclerotic vascular disease, diverticulitis of the colon, and hyperthyroidism. The patient has no previous exposure to other biosimilars and was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications were not reported. The patient began treatment with epoetin zeta (Retacrit; lot number unknown, 27 IU/kg/week, 1 dosage/week, subcutaneous) on 12-Jun-2013 for renal anaemia. The patient was enrolled in the study on 30-Nov-2013. On 09-Feb-2015, the patient experienced lack of efficacy. The patient was admitted from 21-May-2015 until 26-May-2015. On an unknown date, laboratory test results on admission included Hb at 8.1, HTC at 25, MCV at 93.6 (normal values and unit of measurement were not reported) and upon discharge included Hb at 8.1, HTC at 24.8, and MCV at 93. On an unknown date, the patient was diagnosed with stage 4 chronic kidney disease and multifactorial anaemia. During recovery, the patient's antihypertensive therapy was modified; iron and a dose of erythropoietin were administered. Alternative therapy and action taken with the suspect drug were not reported. The event was still ongoing at the time of the report. The patient's weight on discharge was 79.8 kg. The patient's discharged medications were the following: L-Tyrosine 150 mg (1 capsule at 8 from Monday to Saturday), L-Tyrosine (1/2 capsule at 8 on Sunday), Sorbisterit (1 measuring spoonful at lunch, every other day), amlodipine 5 mg (1 capsule at 8am-8pm), Cardioaspirin (1 capsule at lunch), Catapresan TTS (2 on Wednesdays), sodium bicarbonate 500 mg (1 capsule at 8am, midday and 8pm), Sideral Forte (1 capsule at midday), simvastatin 20 mg (1 capsule after dinner), pantoprazole 40 mg (1 capsule at 8am), furosemide 500 mg (1/2 capsule at 8am on Monday and Friday), allopurinol 300mg (1/2 capsule at lunch) Insulin pen (dose not reported) (routes of administration not reported), and low salt diet according to the plan. The reporter's causality assessment for the event and the suspect drug was unlikely. Risk factors included hypertension and type 2 diabetes with diabetic vascular complications. 09-Jun-2015: Additional information was received from the same reporter and English translation of Italian report were received. It has been reported that the patient has no previous exposure to other biosimilars or native ESAs before Retacrit. The patient's weight on discharge was 79.8 kg. Patient's diagnosis, laboratory tests and discharged medications were also provided. Arteriosclerotic vascular disease, diverticulitis of the colon, hyperthyroidism and stage 4 chronic kidney disease were added as concomitant diseases. It was reported that during recovery, the patient's antihypertensive therapy was modified; iron and a dose of erythropoietin were administered. All information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Not assessable As multiple factors can theoretically contribute to the efficacy of this type of medication, cannot provide causation of event without detailed medical history and objective clinical event details, including other causes of anemia (e.g. bleeding) and results of pertinent laboratory results (serial hemoglobin and creatinine levels). Follow-up: Overall case causality: Related Labeled event, but consider also patient comorbidities and reported risk factors. Reporter causality noted.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haematocrit	24.8 Unknown	
2		Haematocrit	25 Unknown	
3		Haemoglobin	8.1 Unknown	
4		Mean cell volume	93 Unknown	
5		Mean cell volume	93.6 Unknown	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	27 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	12-JUN-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		Allergies, alcohol consumption and tobacco usage were not reported. Medical history included diabetic nephropathy which led to renal failure diagnosed in 12-Oct-2004. The patient has been regularly monitored for moderate renal failure, secondary to diabetic nephropathy and cardiovascular disease, in a clinic since 2004. In May of that year, the patient developed anaemia and his renal function worsened. As a consequence, the patient was admitted to hospital. The patient was not on dialysis. Concomitant disease included arteriosclerotic vascular disease, diverticulitis of the colon, and hyperthyroidism. The patient has no previous exposure to other biosimilars and was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Risk factors included hypertension and type 2 diabetes with diabetic vascular complications. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Diverticulitis of colon (without mention of hemorrhage) (Diverticulitis);
Unknown to Ongoing	Relevant Med History	Hyperthyroidism (Hyperthyroidism);
Unknown to Ongoing	Relevant Med History diagnosed in 12-Oct-2004	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Chronic kidney disease stage 4 (Chronic kidney disease);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	MAY	1944	71 Years	Male	88.00 kg	25	MAR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Basal ganglia haemorrhage [Basal ganglia haemorrhage]
Hypertensive crisis [Hypertensive crisis]

Case Description: Basal ganglia haemorrhage and hypertensive crisis. Epoetin zeta. Serious Hospira sponsored clinical study report from Germany, received from an investigator, which refers to a 71-year-old Caucasian male patient (Ge-048-0037; weight:
88 kg also reported as 87.6 kg, height: 170 cm).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 34 IU/Kg/w (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 20-AUG-2014 / 01-MAR-2015

19. THERAPY DURATION
#1) 194 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL DURA (ALLOPURINOL) Tablet ; Unknown
#2) BICANORM (SODIUM BICARBONATE) Tablet ; Unknown
#3) DEKRISTOL (COLECALCIFEROL) Capsule ; Unknown
#4) EXELON /01383201/ (RIVASTIGMINE) Transdermal patch ; Unknown
#5) EXFORGE (AMLODIPINE BESILATE, VALSARTAN) Tablet ; Unknown
#6) KEPPRA (LEVETIRACETAM) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Gonarthrosis (Osteoarthritis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2963426

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-sponsored study entitled Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. He had no history of drug hypersensitivities and drug dependence. Patient medical history included hypertensive nephropathy which led to renal failure diagnosed in 19 Apr 2010 (not on dialysis) also reported as chronic renal insufficiency in stage IV with suspected hypertensive/vascular damage with renal anaemia, beg. metabolic acidosis and mild proteinuria; pronounced cerebral microangiopathy; arterial hypertension with a history of hypertensive crisis in December 2009; incomplete ischaemic insult of the left basal ganglia in December 2009 with latent right-side hemiparesis and remitted dysarthria (in the area of left middle cerebral artery); generalised seizure in 01 Jan 2015; monoclonal gammopathy Type IgG-Kappa; prostate hyperplasia; suspected pathological glucose tolerance; hyperuricaemia; arthritis urica of the right upper ankle joint in December 2009; hyperlipoproteinaemia with hypercholesterolaemia and lipoprotein (a) elevation; class I obesity (BMI 30.31 kg/m^2); coxarthrosis on the right with TEP in 22 Oct 2013; GI bleeding in 04 Apr 2013 (unclear source of blood) and beginning gonarthrosis on the left. The patient has not been treated with other erythropoiesis stimulating agent (ESA) prior to this study. Concomitant medications included simvastatin Axcount coated tablets (40 mg, 1/2 dosage form, once a day; reduced to 10 mg, once a day), allopurinol Dura tablets (300 mg, once a day; reduced to 200 mg, once a day), Exforge coated tablets (5 mg/80 mg, 1 dosage form, once a day), furosemide 40 Heumann tablet Heunet (40 mg, once a day), ASA 100 1A Pharma tablets (100 mg, once a day), Nebilet tablets (6 mg, twice a day), Dekristol soft capsules (20,000 IU, 1 caps, every 7 days on Wednesdays), pantoprazole 1A Pharma enteric-coated tablets (Pantozol, 20 mg, once a day), Bicanorm enteric-coated tablets (1 dosage form, once a day), venlafaxine 1 A Pharma 37.5 mg tablets (37.5 mg, thrice a day), Exelon transdermal patch (4.6 mg/24 hours), valproic acid Ratioph 600 enteric-coated tablets (1 dosage form, twice a day), Keppra (500 mg, twice a day), Novaminosulfone (500 mg, twice a day) (routes of administration not reported) for unknown indications, heparin (5000 IU, twice a day, subcutaneous) for an unknown indication, and lorazepam Dura tablets (1mg, in the event of seizure aura, route of administration not reported) for seizure. On 20 Aug 2014, the patient started treatment with epoetin zeta injection solution (Retacrit, 34 IU/kg/week, also reported as 3000 IU/0.9 mL, 1 injection/week on Fridays; subcutaneous; lot number not available) for renal anaemia. Informed consent was signed on 15 Jan 2015. On 25 Mar 2015, the patient experienced basal ganglia haemorrhage on the right (putamen and external capsule) and hypertensive crisis (associated with known arterial hypertension). It was reported that the patient was admitted to the hospital due to acute slowdown and disorientation. Computer tomography indicated intracerebral haemorrhage in the region of the right basal ganglia occurring with the use of aspirin. Specifically on the same day of 25 Mar 2015, imaging showed a fully 3 cm intracranial haemorrhage in the right external capsule with perifocal oedema, s/p high-parietal partial left medial infarction, and advanced leukoencephalopathy. On 26 Mar 2015, compared to the previous image taken on the preceding day, the right central hypertensive basal ganglia haemorrhage in the region of the putamen showed no increase in size at a maximum breadth of 3.2 cm; hence, there was no indication of interim secondary haemorrhage. In addition, there was no indication of rupture into the ventricle. There was a slight increase of the still small perifocal oedema with only local moderate spaceoccupying effect on the adjacent right anterior horn of the lateral ventricle. There was also unchanged evidence of a lacunar defect left central in the region of the internal capsule with evacuating ballooning of the left anterior horn of the lateral ventricle and an older, somewhat cystic collocated, somewhat gliomatous transformed, larger and older partial medial infarction of the left parieto-occiptal in the region of the posterior border zone of the middle cerebral flow area. And finally a slightly enhanced hypodense density reduction of the periventricular white matter in the context of a vascular leukoencephalopathy. Magnetic resonance imaging revealed a similar picture of organic brain structures as the known computer tomography. Image of the large right central basal ganglia haemorrhage in the putamen was unchanged, with small perifocal oedema and impression of the right lateral ventricle. Likewise, the residual traces of the left parieto-occipital media infarction and the lacuna of the left central area of the thalamus appear similar. As was typical, the described vascular leukoencephalopathy was somewhat clearer in the MRI. There was no new ischaemic oedema formation with diffusion weighting. With respect to the clinical question of an amyloid angiopathy, in addition to the new right central hypertensive bleeding there was only one small micro bleed reflecting residual bleeding on the right in the region of the cerebral peduncle. A second discrete micro bleed can be seen in the white matter of the left periventricular region. Hence, these minor changes still do not provide conclusive evidence for the diagnosis of an amyloid angiopathy. Overall, imaging showed that the haemorrhage was stable over the course of time, and MRI confirmed the bleeding; however, there was no suspicion of an amyloid angiopathy. Doppler Sonography was also conducted which showed cardiac arrhythmia; trantemporal: MCA, ACA, PCA on both sides; vertebrobasilar: VAR < VAL, VAR not well displayed; basilar artery: not well displayed (up to 104 mm deep); and overall no evidence of haemodynamically-relevant stenoses. Neurological findings showed that the patient was conscious, fully oriented, friendly and approachable on communication. There was no indication of formal or substantive thought disturbances, headache, meningism, aphasia, but there was slight residual dysarthria. Cerebral nerve status showed pupils round and equally dilated, normal direct and consensual response to light on both sides, saccadic pursuit, no weakness of the buccal branch of the facial nerve, and caudal cerebral nerves were also normal. Motor function showed no manifest or latent paresis, proprioceptive reflex equal on both sides and moderate; Babinski reflex negative on both sides, and arm extension test and leg extension tests were normal. Standing was possible but unstable with 2 people assisting; and gait was possible for a few steps but unsteady with 2 people assisting. There was sensitivity with a slight pallhypaesthesia of 5/8 bimalleolar on both sides, otherwise intact. Psychological findings showed that the patient was somnolent but can be immediately roused, and roughly oriented in all respects. CCT on 27 Mar 2015 showed that, compared to previous images, there was no indicative change in the findings with respect to the right central basal ganglia haemorrhage and the previous ischemia residual. The hypertensive crisis improved with the administration of Ebrantil (30 mg, thrice a day; route of administration not reported), this was thus included with

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

his antihypertensive medications. Later, ramipril (renal dose of 1.25 mg, in the mornings, route of administration not reported) was administered. Aspirin was stopped and it was advised that this can be resumed if necessary after resorption of the haemorrhage as long as the blood pressure does not go below 140/90 for a prolonged period. The patient's clinical signs improved, so that he can be mobilised into the chair and was sufficiently oriented, although still slow. Rehabilitation was set up. The doses of some medications were also adjusted because of the known renal insufficiency. Retacrit therapy was interrupted by the patient since his hospitalization in March 2015. On 04 Apr 2015, the patient had recovered with sequelae from the event. The investigator considered the events unlikely related to Retacrit. According to the investigator, the patient had been on Retacrit since 20 Aug 2014 with no reaction. Risk factors included stroke, hyperlipidaemia, and hypertension. 06 Aug 2015: English translation of the discharge summary was received. Event terms were updated to basal ganglia haemorrhage and hypertensive crisis (previously basal ganglia bleeding and hypertensive episode, respectively), and coded accordingly. Complete medical history was provided. Additional event details including complete relevant laboratory tests and treatment for the events were provided. Additional concomitant medication information including formulations, doses for ASA, furosemide, Nebilet, decristol, and Exelon, lorazepam dose and indication, and translation for valproinsaeure were provided; heparin, Keppra and Novaminsulfone were also added. This information has been incorporated in the narrative and the corresponding data fields. The reporter was unable to provide the following information for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars.

Case Comment: Overall case causality: Probably not (Reporter's causality: Unlikely) Hospira causality: Not related Though temporally related and labeled with Retacrit, the events are more likely associated to the patient's underlying conditions. Followup: Additional event details noted. No change in causality assessment

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Babinski reflex test	Negative on both sides Unknown	
2		Body mass index	30.31 kg/m^2 Unknown	
3	25-MAR-2015	Computerised tomogram head	Advanced leukoencephalopathy, Unknown	
4	25-MAR-2015	Computerised tomogram head	With perifocal oedema Unknown	
5	25-MAR-2015	Computerised tomogram head	3 cm hemorrhage (right external capsule) Unknown	
6	25-MAR-2015	Computerised tomogram head	S/P high-parietal partial left medial infarction U	
7	25-MAR-2015	Computerised tomogram head	Intracerebral haemorrhage (right basal ganglia) Un	
8	26-MAR-2015	Computerised tomogram head	Maximum breadth: 3.2 CM	
9	26-MAR-2015	Computerised tomogram head	No indication of rupture into the ventricle Unknow	
10	26-MAR-2015	Computerised tomogram head	No indication of interim secondary haemorrhage Unk	
11	26-MAR-2015	Computerised tomogram head	Slight density reduction of white matter Unknown	
12	26-MAR-2015	Computerised tomogram head	Haemorrhage showed no increase in size Unknown	
13	26-MAR-2015	Computerised tomogram head	Unchanged evidence of older infarction Unknown	
14	26-MAR-2015	Computerised tomogram head	In the context of a vascular leukoencephalopathy U	
15	26-MAR-2015	Computerised tomogram head	Slight increase of the small perifocal oedema	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			Unkn	
16	27-MAR-2015	Computerised tomogram head	No change in the findings with respect to events U	
17		Magnetic resonance imaging brain	Similar results as the computer tomography Unknown	
18		Magnetic resonance imaging brain	Residual traces of the left POM infarction Unknown	
19		Magnetic resonance imaging brain	No new ischemic edema formation Unknown	
20		Magnetic resonance imaging brain	No conclusive evidence of amyloid angiopathy Unkno	
21		Magnetic resonance imaging brain	Discrete micro bleed in L periventricular region U	
22		Magnetic resonance imaging brain	Clearer image of the vascular leukoencephalopathy	
23		Magnetic resonance imaging brain	Basal ganglia haemorrhage was unchanged Unknown	
24		Magnetic resonance imaging brain	With small perifocal oedema Unknown	
25		Magnetic resonance imaging brain	Residual micro bleed on the R cerebral peduncle Un	
26		Magnetic resonance imaging brain	Lacuna of the thalamus appear similar Unknown	
27		Nerve stimulation test	Caudal cerebral nerves were normal Unknown	
28		Nerve stimulation test	Saccadic pursuit Unknown	
29		Nerve stimulation test	No weakness of buccal branch of the facial nerve U	
30		Neurological examination	Standing possible but unstable; 2 people assisting	
31		Neurological examination	Slight pallhypaesthesia of 5/8 bimalleolar Unknown	
32		Neurological examination	No aphasia; With slight residual dysarthria Unknow	
33		Neurological examination	Gait possible for a few steps bu unsteady Unknown	
34		Neurological examination	Bimalleolar otherwise intact Unknown	
35		Neurological examination	Proprioceptive reflex equal/moderate (both sides),	
36		Neurological examination	Arm extension and leg extension tests normal Unkno	
37		Neurological examination	No manifest or latent	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			paresis Unknown	
38		Neurological examination	Conscious, fully oriented, friendly, approachable,	
39		Neurological examination	No thought disturbances, headache, meningism Unkno	
40		Neuropsychological test	Roughly oriented in all respects Unknown	
41		Neuropsychological test	Somnolent, but can be immediately roused Unknown	
42		Pupillary light reflex tests	Normal response to light on both sides Unknown	
43		Pupillary light reflex tests	Pupils round and equally dilated Unknown	
44		Ultrasound Doppler	Cardiac arrhythmia Unknown	
45		Ultrasound Doppler	No evidence of haemodynamicallyrelevant stenoses U	

13. Relevant Tests

Cerebral nerve status (Unknown date): No weakness of buccal branch of the facial nerve, Unknown
Computer tomography (Unknown date): Intracerebral haemorrhage (right basal ganglia), Unknown
Computer tomography (Unknown date): S/P high-parietal partial left medial infarction, Unknown
Computer tomography (Unknown date): In the context of a vascular leukoencephalopathy Unknown
Computer tomography (Unknown date): No indication of interim secondary haemorrhage Unknown
Computer tomography (Unknown date): No indication of rupture into the ventricle Unknown
Computer tomography (Unknown date): Slight increase of the small perifocal oedema Unknown
Computer tomography (Unknown date): No change in the findings with respect to events Unknown
Magnetic resonance imaging (Unknown date): Clearer image of the vascular leukoencephalopathy Unknown
Magnetic resonance imaging (Unknown date): Discrete micro bleed in L periventricular region Unknown
Magnetic resonance imaging (Unknown date): No conclusive evidence of amyloid angiopathy Unknown
Magnetic resonance imaging (Unknown date): Residual micro bleed on the R cerebral peduncle Unknown
Motor function (Unknown date): Arm extension and leg extension tests normal Unknown
Motor function (Unknown date): Proprioceptive reflex equal/moderate (both sides), Unknown
Neurological findings (Unknown date): Conscious, fully oriented, friendly, approachable, Unknown
Neurological findings (Unknown date): No aphasia; With slight residual dysarthria Unknown
Neurological findings (Unknown date): No thought disturbances, headache, meningism Unknown
Neurological findings (Unknown date): Standing possible but unstable; 2 people assisting Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	34 IU/Kg/week, Freq:1 week, interval:1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	20-AUG-2014 / 01-MAR-2015; 194 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LORAZEPAM DURA (LORAZEPAM) Tablet ; Unknown

#8) NEBILET (NEBIVOLOL HYDROCHLORIDE) Tablet ; Unknown

#9) NOVAMINSULFON (METAMIZOLE SODIUM) ; Unknown

#10) PANTOZOL /01263204/ (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#11) ASA (ACETYLSALICYLIC ACID) Tablet ; Unknown

#12) FUROSEMIDE (FUROSEMIDE) ; Unknown

#13) HEPARIN (HEPARIN) ; Unknown

#14) SIMVASTATIN (SIMVASTATIN) Tablet ; Unknown

#15) VALPROIC ACID (VALPROIC ACID) Tablet ; Unknown

#16) VENLAFAXINE (VENLAFAXINE) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Tobacco usage and alcohol consumption were not reported. He had no history of drug hypersensitivities and drug dependence. Patient medical history included hypertensive nephropathy which led to renal failure diagnosed in 19 Apr 2010 (not on dialysis) also reported as chronic renal insufficiency in stage IV with suspected hypertensive/vascular damage with renal anaemia, beg. metabolic acidosis and mild proteinuria; pronounced cerebral microangiopathy; arterial hypertension with a history of hypertensive crisis in December 2009; incomplete ischaemic insult of the left basal ganglia in December 2009 with latent right-side hemiparesis and remitted dysarthria (in the area of left middle cerebral artery); generalised seizure in 01 Jan 2015; monoclonal gammopathy Type IgG-Kappa; prostate hyperplasia; suspected pathological glucose tolerance; hyperuricaemia; arthritis urica of the right upper ankle joint in December 2009; hyperlipoproteinaemia with hypercholesterolaemia and lipoprotein (a) elevation; class I obesity (BMI 30.31 kg/m^2); coxarthrosis on the right with TEP in 22 Oct 2013; GI bleeding in 04 Apr 2013 (unclear source of blood) and beginning gonarthrosis on the left. The patient has not been treated with other erythropoiesis stimulating agent (ESA) prior to this study. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Metabolic acidosis (Metabolic acidosis);
Unknown to Ongoing	Relevant Med History	Obesity (Obesity);
Unknown to Ongoing	Relevant Med History	Coxarthrosis (Osteoarthritis);
Unknown to Ongoing	Relevant Med History	Hypercholesterolaemia (Hypercholesterolaemia);
Unknown to Ongoing	Relevant Med History	Hyperlipoproteinaemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Hyperuricaemia (Hyperuricaemia);
Unknown to Ongoing	Relevant Med History	Hemiparesis (right) (Hemiparesis);
Unknown to Ongoing	Relevant Med History	Proteinuria (Proteinuria);
Unknown to Ongoing	Relevant Med History	IgG gammopathy (Monoclonal gammopathy);
Unknown to Ongoing	Relevant Med History	Cerebral microangiopathy (Cerebral microangiopathy);
Unknown to Ongoing	Relevant Med History	Prostatic hyperplasia (Benign prostatic hyperplasia);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Dysarthria (Dysarthria);
Unknown to Ongoing	Relevant Med History Diagnosed in 19 Apr 2010	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Glucose tolerance impaired (Glucose tolerance impaired);
Unknown	Relevant Med History In December 2009	Hyperuricaemic arthritis (Gouty arthritis);
Unknown	Relevant Med History In 22 Oct 2013	Prosthesis implantation (Prosthesis implantation);
Unknown	Relevant Med History In 01 Jan 2015	Seizure (Seizure);
Unknown	Relevant Med History In 04 Apr 2013	GI bleed (Gastrointestinal haemorrhage);
Unknown	Relevant Med History In December 2009	Hypertensive crisis (Hypertensive crisis);
Unknown	Relevant Med History	Hypertension arterial (Hypertension);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History In December 2009	Ischaemic stroke (Ischaemic stroke);
Unknown	Relevant Med History Concurrent condition	Cardiac arrhythmia (Arrhythmia);
Unknown	Relevant Med History Concurrent condition	Leukoencephalopathy (Leukoencephalopathy);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	01	JUL	1931	84 Years	Female	79.50 kg	30	APR	2015	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Chronic atrial fibrillation [Atrial fibrillation]
NSTEMI due to acute, proximal occlusion of the RCX [Acute myocardial infarction]
Pericardial effusion [Pericardial effusion]
Residual severe stenosis of the RIVP and the RIVA [Coronary artery stenosis]

Case Description: Pericardial effusion, chronic atrial fibrillation, residual severe stenosis of the RIVP and the RIVA, and NSTEMI due to

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 150.9 IU/kg/wek, 3 doses/wk

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 06-JAN-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown		()

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2971062

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-MAR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

acute, proximal occlusion of the RCX. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (ref: Ge-093-0076), which refers to an 84-year-old (also reported as 83-year-old) Caucasian female patient (height: 165 cm, dry weight: 79.5 kg, also reported as 73 kg). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had an allergy to penicillin. The patient was not pregnant and lactating at the time of the report. The patient had nephrosclerosis and abuse of analgesics which led to renal failure, also reported as chronic renal insufficiency requiring dialysis stage III, diagnosed on 24-Sep-2013. The patient was subjected to hemodialysis and was started on 08-Jan-2014 with an average frequency of 3 times per week (Monday, Wednesday, Friday). The patient was not treated with Erythropoiesis-Stimulating Agent (ESA) prior to treatment with Retacrit. Medical history included GORD and s/p appendectomy (1979). Concomitant medications were not reported. On 08-Jan-2014, the patient began treatment with epoetin zeta (Retacrit, 150.9 IU/kg, 3 doses/week, also reported as once/week, subcutaneous, lot number unknown) for renal anemia. On 01-Feb-2014, the patient was enrolled in the study. It was reported that the date of last dose of Retacrit prior to the event was on 27-Aug-2014. On an unknown date, an echocardiogram revealed a pericardial effusion of a maximum 18 mm end-diastolic widening before the LV, 10 mm before the RV from subcostal. Following a conversation with the dialysis center, it was learned that a significant pericardial effusion was noted there already as an incidental finding in an abdominal CT on 30-Apr-2015. A TTE on 01 Jun 2015 confirmed a circular effusion of 14 mm. The pericardial effusion appears to be chromic in origin and had not increased in size and was currently not haemodynamically relevant. On 01-Jun-2015, laboratory results showed leukocytes 8.7 x 10^3/MCL (normal range: 4.3-10 thousands/MCL), thrombocytes 207 x 10^3/MCL (normal range: 150-400 thousands/MCL), haemoglobin 13.3 g/dL (normal range: 12-16 g/dL), haematocrit 39.1% (normal range: 37-47 %), ferritin 708 ng/mL (normal range: 13-150 ng/mL), CRP (sensitive) 0.6 mg/dL (normal range: 0-0.5 mg/dL), phosphate in serum 3.2 mg/dL (normal range: 2.5-4.5 mg/dL), calcium in serum 2.22 mmol/dL (normal range: 2.00-2.8 mmol/dL), PTH intact 113 pg/mL (normal range: 10-65), absolute albumin 3.6 g/dL (normal range: 3500-5500 g/dL), and Kt/V acc. To Daugirdas 3.33 (normal range not reported). On 02-Jul-2015, the patient was admitted as an inpatient on an emergency basis due to anginous pain that was present since the day prior to the date of admission. Physical examination findings on admission included the following: good, stable overall condition appropriate for age and slightly over-nourished nutritional state (150 cm, 74 kg); alert, oriented to person, time, place and situation, basic neurological orientation was normal; no dyspnea, no cyanosis, slight lower leg oedema, no icterus. Pupils: both round, equally dilated, responding to direct and indirect light; head and neck with basic orientation normal; pulmonary: ventilated equally on both sides, both lung borders displaced on respiration, sonorous percussion sound, vesicular breath sounds, no crackling sounds; Coronary: pure heart tones, arrhythmic, no pathological sounds, central and peripheral pulse; Abdomen: soft, borborygmus normal in all four sections, no pain on palpitation, no muscular guarding, no resistances, liver and spleen not palpably enlarged; Kidney region: no pain on percussion; Spinal colums: no pain on percussion; peripheral pulse normal, no carotid or femoral bruits; Allen test: normal both sides; no calf compression pan; no hepatojugular reflux. Resting ECG on 02-Jul-2015 showed absolute arrhythmia associated with atrial fibrillation, normal heart rate transition at 80 bpm, intermediate heart, normal conduction times, discreet ST segment depressions V3-V5/II/aVF, normal R-progression, R/S transition in V2, prominent S up to V6. Radiological evidence ruled out congestion, infiltrate or pleural effusion. Laboratory chemistry results and electrocardiographic findings on an unknown date indicated to the general practitioner configuration of NSTEMI; with persisting symptoms, a coronary angiograph was therefore immediately performed. It was followed by implantation of a PTCA and DE stent (Synsiro 2.75 x 22 mm) in the region of the proximal occluded RCx. The patient was then admitted to the intensive care ward after the intervention for ongoing monitoring. The patient was transferred in stable condition to the peripheral ward on 03 Jul 2015. Resting ECG on 03-Jul-2015 showed consistent findings with resting ECG from previous day, ST segment depressions in chest leads were declining. Coronary angiography on 03-Jul-2015 showed HS: sclerotic, no significant stenosis; RIVA: 50% stenosis at the origin from the main stem, TIMI III flow toward distal; RCX: severe stenosis proximally at the origin from the HS taking into account the M1, functional occlusion; RCA: diffuse sclerosis, extremely stenosed at the origin of the RIVP, TIMI III flow toward distal. Severe arrhythmia was not documented on the telemetric monitoring or the long-term ECG. Follow-up treatment was requested through social services. On an unknown date, the patient was then diagnosed with NSTEMI due to acute, proximal occlusion of the RCX, chronic atrial fibrillation, and residual severe stenosis of the RIVP and the RIVA (50%). With a post-intervention period that proceeded without complication, the patient was discharged on 07-Jul-2015 to follow-up patient care. On 12-Jul-2015, as management for chronic atrial fibrillation the patient underwent cardioversion and received anticoagulant (Marcumar; oral, dose not reported), with EHRA:1 CHADS-VASc:4, and HAS-BLED:2. On 13-Jul-2015, laboratory results showed leukocytes 8.2 x 10^3/MCL (normal range: 4.3-10 thousands/MCL), thrombocytes 238 x 10^3/UL (normal range: 150-400 thousands/MCL), ferritin 965 ng/mL (normal range: 13-150 ng/mL), phosphate in serum 3 mg/dL (normal range: 2.5-4.5 mg/dL), potassium in serum 3.8 mmol/dL (normal range: 3.7-5.0 mmol/dL), and PTH intact 171 pg/mL (normal range: 10-65). On 06-Aug-2015, as management for NSTEMI the patient underwent bifurcation PTCA LAD/D1 with DES stent implantation. Final treatment recommendations included optimizing the cardiovascular risk profile and request a triple therapy (ASA, clopidogrel and Phenprocoumon; doses and routes of administration) for at least 6 months after the implant of the stent and followed by a dual therapy (ASA + Phenprocoumon or Clopidogrel + Phenprocoumon); optimizing the dose of Marcumar to achieve a target INR of 2-3 with appropriate regular INR monitoring; regular monitoring of potassium; and regular monitoring of pericardial effusion using TTE. It was also reported that an appointment for patient admission as an inpatient to carry out a re-coronary angiography with PTCA of the RIVP was arranged, if necessary in 6 weeks. Medication on discharge included ASA (100 mg for life), clopidogrel zentiva 75 (Plavix; 75 mg for 6 months), Marcumar (target INR 2-3, 1 ½ tablets; dose not reported), Pantozol (40 mg), metoprolol succinate (47.5 mg), water pill (Lasix; 250mg), atorvastatin 40

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(Sortis; 60 mg), prednisolone (5 mg), Novalgin (500 mg), Fentanyl TTS (25 mcg/h every 3 days alternating) (routes of administration not reported) all given for unknown indications. Treatment for the events of pericardial effusion and residual severe stenosis of the RIVP and the RIVA, action taken with the suspect drug and outcome of the events were not reported. The investigator's opinion of causality between the adverse events and the suspect drug was not reported. Risk factors included arterial hypertension, colon cancer diagnosed on an unknown day in Nov-2012, obesity, hyperlipoproteinaemia, positive family history for cardiovascular disease, ongoing nicotine abuse. 13-Aug-2015: English translation of patient's discharge summary in German text was received. Pericardial effusion; chronic atrial fibrillation; residual severe stenosis of the RIVP and the RIVA; and NSTEMI due to acute, proximal occlusion of the RCX were added as adverse events. Thromboembolic event was removed as an event. Hospitalisation was added as seriousness criterion. Allergy to penicillin, GORD, and s/p appendectomy were added medical history. Further medical history details were also provided. Obesity, hyperlipoproteinaemia, positive family history for cardiovascular disease, ongoing nicotine abuse were added as risk factors. Laboratory/diagnostic data, medical and surgical procedures, treatment for the adverse events, and further adverse event details were provided. This information has been incorporated in the narrative and in corresponding data fields. The reporter was unable to provide the following information for identification and traceability of the biosimilar product epoetin zeta (Retacrit): batch number, date of expiry and previous exposure of patient to other biosimilars.

PRD: (04-Mar-2016) SRD : (05-Mar-2016)
Pericardial effusion, chronic atrial fibrillation, residual severe stenosis of the RIVP and the RIVA, and NSTEMI due to acute, proximal occlusion of the RCX. Epoetin zeta. Serious Hospira-sponsored study report from Germany, received from an investigator (ref: Ge-093-0076), which refers to an 84-year-old (also reported as 83-year-old) Caucasian female patient (height: 165 cm, dry weight: 79.5 kg, also reported as 73 kg). The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had an allergy to penicillin. The patient was not pregnant and lactating at the time of the report. The patient had nephrosclerosis and abuse of analgesics which led to renal failure, also reported as chronic renal insufficiency requiring dialysis stage III, diagnosed on 24-Sep-2013. The patient was subjected to hemodialysis and was started on 08-Jan-2014 with an average frequency of 3 times per week (Monday, Wednesday, Friday). The patient was not treated with Erythropoiesis-Stimulating Agent (ESA) prior to treatment with Retacrit. Medical history included GORD and s/p appendectomy (1979), hyperlipidemia, ischemic heart disease three-vessel-disease and atrial fibrillation. Concomitant medications were not reported. On 08-Jan-2014, the patient began treatment with epoetin zeta (Retacrit, 150.9 IU/kg, 3 doses/week, also reported as once/week, subcutaneous, lot number unknown) for renal anemia. On 01-Feb-2014, the patient was enrolled in the study. It was reported that the date of last dose of Retacrit prior to the event was on 27-Aug-2014. On 13-Apr-2015, haemoglobin was 13.1 g/dL. On an unknown date, an echocardiogram revealed a pericardial effusion of a maximum 18 mm end-diastolic widening before the LV, 10 mm before the RV from subcostal. Following a conversation with the dialysis center, it was learned that a significant pericardial effusion was noted there already as an incidental finding in an abdominal CT on 30-Apr-2015. A TTE on 01 Jun 2015 confirmed a circular effusion of 14 mm. The pericardial effusion appears to be chromic in origin and had not increased in size and was currently not haemodynamically relevant. On 01-Jun-2015, laboratory results showed leukocytes 8.7 x 10^3/MCL (normal range: 4.3-10 thousands/MCL), thrombocytes 207 x 10^3/MCL (normal range: 150-400 thousands/MCL), haemoglobin 13.3 g/dL (normal range: 12-16 g/dL), haematocrit 39.1% (normal range: 37-47 %), ferritin 708 ng/mL (normal range: 13-150 ng/mL), CRP (sensitive) 0.6 mg/dL (normal range: 0-0.5 mg/dL), phosphate in serum 3.2 mg/dL (normal range: 2.5-4.5 mg/dL), calcium in serum 2.22 mmol/dL (normal range: 2.00-2.8 mmol/dL), PTH intact 113 pg/mL (normal range: 10-65), absolute albumin 3.6 g/dL (normal range: 3500-5500 g/dL), and Kt/V acc. To Daugirdas 3.33 (normal range not reported). On 02-Jul-2015, the patient was admitted as an inpatient on an emergency basis due to anginous pain that was present since the day prior to the date of admission. Physical examination findings on admission included the following: good, stable overall condition appropriate for age and slightly over-nourished nutritional state (150 cm, 74 kg); alert, oriented to person, time, place and situation, basic neurological orientation was normal; no dyspnea, no cyanosis, slight lower leg oedema, no icterus. Pupils: both round, equally dilated, responding to direct and indirect light; head and neck with basic orientation normal; pulmonary: ventilated equally on both sides, both lung borders displaced on respiration, sonorous percussion sound, vesicular breath sounds, no crackling sounds; Coronary: pure heart tones, arrhythmic, no pathological sounds, central and peripheral pulse; Abdomen: soft, borborygmus normal in all four sections, no pain on palpitation, no muscular guarding, no resistances, liver and spleen not palpably enlarged; Kidney region: no pain on percussion; Spinal colums: no pain on percussion; peripheral pulse normal, no carotid or femoral bruits; Allen test: normal both sides; no calf compression pan; no hepatojugular reflux. Resting ECG on 02-Jul-2015 showed absolute arrhythmia associated with atrial fibrillation, normal heart rate transition at 80 bpm, intermediate heart, normal conduction times, discreet ST segment depressions V3-V5/II/aVF, normal R-progression, R/S transition in V2, prominent S up to V6. Radiological evidence ruled out congestion, infiltrate or pleural effusion. Laboratory chemistry results and electrocardiographic findings on an unknown date indicated to the general practitioner configuration of NSTEMI; with persisting symptoms, a coronary angiograph was therefore immediately performed. It was followed by implantation of a PTCA and DE stent (Synsiro 2.75 x 22 mm) in the region of the proximal occluded RCx. The patient was then admitted to the intensive care ward after the intervention for ongoing monitoring. The patient was transferred in stable condition to the peripheral ward on 03 Jul 2015. Resting ECG on 03-Jul-2015 showed consistent findings with resting ECG from previous day, ST segment depressions in chest leads were declining. Coronary angiography on 03-Jul-2015 showed HS: sclerotic, no significant stenosis; RIVA: 50% stenosis at the origin from the main stem, TIMI III flow toward distal; RCX: severe stenosis proximally at the origin from the HS taking into account the M1, functional occlusion; RCA: diffuse sclerosis, extremely stenosed at the origin of the RIVP, TIMI III flow toward distal. Severe arrhythmia was not documented on the telemetric monitoring or the long-term ECG. Follow-up treatment was requested through social services. On 02-Jul-2015, the patient

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

was then diagnosed with NSTEMI due to acute, proximal occlusion of the RCX, chronic atrial fibrillation, and residual severe stenosis of the RIVP and the RIVA (50%). With a post-intervention period that proceeded without complication, the patient was discharged on 07-Jul-2015 to follow-up patient care. On 07-Jul-2015, the patient recovered from the event of NSTEMI. On 12-Jul-2015, as management for chronic atrial fibrillation the patient underwent cardioversion and received anticoagulant (Marcumar; oral, dose not reported), with EHRA:1 CHADS-VASc:4, and HAS-BLED:2. On 13-Jul-2015, laboratory results showed leukocytes 8.2 x 10^3/MCL (normal range: 4.3-10 thousands/MCL), thrombocytes 238 x 10^3/UL (normal range: 150-400 thousands/MCL), ferritin 965 ng/mL (normal range: 13-150 ng/mL), phosphate in serum 3 mg/dL (normal range: 2.5-4.5 mg/dL), potassium in serum 3.8 mmol/dL (normal range: 3.7-5.0 mmol/dL), and PTH intact 171 pg/mL (normal range: 10-65). On 06-Aug-2015, as management for NSTEMI the patient underwent bifurcation PTCA LAD/D1 with DES stent implantation. Final treatment recommendations included optimizing the cardiovascular risk profile and request a triple therapy (ASA, clopidogrel and Phenprocoumon; doses and routes of administration) for at least 6 months after the implant of the stent and followed by a dual therapy (ASA + Phenprocoumon or Clopidogrel + Phenprocoumon); optimizing the dose of Marcumar to achieve a target INR of 2-3 with appropriate regular INR monitoring; regular monitoring of potassium; and regular monitoring of pericardial effusion using TTE. It was also reported that an appointment for patient admission as an inpatient to carry out a re-coronary angiography with PTCA of the RIVP was arranged, if necessary in 6 weeks. Medication on discharge included ASA (100 mg for life), clopidogrel zentiva 75 (Plavix; 75 mg for 6 months), Marcumar (target INR 2-3, 1 1/2 tablets; dose not reported), Pantozol (40 mg), metoprolol succinate (47.5 mg), water pill (Lasix; 250mg), atorvastatin 40 (Sortis; 60 mg), prednisolone (5 mg), Novalgin (500 mg), Fentanyl TTS (25 mcg/h every 3 days alternating) (routes of administration not reported) all given for unknown indications. Treatment for the events of pericardial effusion and residual severe stenosis of the RIVP and the RIVA, action taken with the suspect drug and outcome of the events (except for NSTEMI) were not reported. The investigator's opinion of causality between the event of NSTEMI and the suspect drug was not related. The investigator's opinion of causality between the other adverse events (pericardial effusion, chronic atrial fibrillation, residual severe stenosis of the RIVP and the RIVA) and the suspect drug was not reported. Risk factors included arterial hypertension, colon cancer diagnosed on an unknown day in Nov-2012, obesity (BMI: 26.81), hyperlipoproteinaemia, positive family history for cardiovascular disease, ongoing nicotine abuse, smoking (packs per day UK), . 13-Aug-2015: English translation of patient's discharge summary in German text was received. Pericardial effusion; chronic atrial fibrillation; residual severe stenosis of the RIVP and the RIVA; and NSTEMI due to acute, proximal occlusion of the RCX were added as adverse events. Thromboembolic event was removed as an event. Hospitalisation was added as seriousness criterion. Allergy to penicillin, GORD, and s/p appendectomy were added medical history. Further medical history details were also provided. Obesity, hyperlipoproteinaemia, positive family history for cardiovascular disease, ongoing nicotine abuse were added as risk factors. Laboratory/diagnostic data, medical and surgical procedures, treatment for the adverse events, and further adverse event details were provided. This information has been incorporated in the narrative and in corresponding data fields. The reporter was unable to provide the following information for identification and traceability of the biosimilar product epoetin zeta (Retacrit): batch number, date of expiry and previous exposure of patient to other biosimilars. 04 Mar 2016: Additional information was received from the same reporter. Smoking (packs per day UK) and obesity with BMI: 26.81 were added as risk factors. Hyperlipidemia, ischemic heart disease (three-vessel-disease) and atrial fibrillation were added as medical history. Reaction start and stop dates, outcome and reporter's opinion of causality for event NSTEMI were also provided. On 13-Apr-2015, haemoglobin was 13.1 g/dL. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable While a labeled event, cannot provide event causation without a firm timeline, clinical course, objective clinical event details, medical history and concomitant medications. Follow-up: Overall case causality: Related Chronic atrial fibrillation is not related as this is more likely a pre-existing condition. The remaining events are related. Labeled events or in the spectrum of potential sequelae from labeled events, and possible sequela, but consider also reported risk factors (arterial hypertension, undelrying malignancy, obesity, hyperlipoproteinaemia, positive family history and drug abuse).

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-APR-2015	Abdomen scan	Significant pericardial effusion, Unknown	
2	03-JUL-2015	Angiocardiogram	Functional occlusion, Unknown	
3	03-JUL-2015	Angiocardiogram	TIMI III flow toward distal, Unknown	
4	03-JUL-2015	Angiocardiogram	RCA: diffuse sclerosis, Unknown	
5	03-JUL-2015	Angiocardiogram	HS: sclerotic, no significant stenosis, Unknown	
6	03-JUL-2015	Angiocardiogram	From the HS taking into account the M1, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	03-JUL-2015	Angiocardiogram	RCX: severe stenosis proximally at the origin, Unk	
8	03-JUL-2015	Angiocardiogram	RIVA: 50% stenosis at the origin from main stem,	
9	01-JUN-2015	Blood albumin	3.6 g/dl	5500 3500
10	01-JUN-2015	Blood calcium	2.22, MMOL/DL	2.8 2.00
11	01-JUN-2015	Blood parathyroid hormone	113, PG/ML	65 10
12	13-JUL-2015	Blood parathyroid hormone	171, PG/ML	65 10
13	01-JUN-2015	Blood phosphorus	3.2 mg/dl	4.5 2.5
14	13-JUL-2015	Blood phosphorus	3 mg/dl	4.5 2.5
15	13-JUL-2015	Blood potassium	3.8, MMOL/DL	2.8 2.00
16		Body mass index	26.81, Unknown	
17	01-JUN-2015	C-reactive protein	0.6 mg/dl	0.5 0
18	02-JUL-2015	Cardiovascular examination	Pure heart tones, arrhythmic, Unknown	
19	02-JUL-2015	Cardiovascular examination	No pathological sounds, Unknown	
20	02-JUL-2015	Cardiovascular examination	Central and peripheral pulse, Unknown	
21	30-APR-2015	Computerised tomogram abdomen	Significant pericardial effusion,Unknown	
22		Diagnostic procedure	Ruled out leural effusion, Unknown	
23		Diagnostic procedure	Ruled out congestion, infiltrate, Unknown	
24	01-JUN-2015	Dialysis efficacy test	3.33, Unknown	
25		Echocardiogram	Pericardial effusion, Unknown	
26	01-JUN-2015	Echocardiogram	Circular effusion of 14 mm, Unknown	
27		Electrocardiogram	Configuration of NSTEMI, Unknown	
28	02-JUL-2015	Electrocardiogram	Absolute arrhythmia, Unknown	
29	02-JUL-2015	Electrocardiogram	Prominent S up to V6, Unknown	
30	02-JUL-2015	Electrocardiogram	Associated with atrial fibrillation, Unknown	
31	02-JUL-2015	Electrocardiogram	Normal R-progression, R/S transition in V2,Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
32	02-JUL-2015	Electrocardiogram	Normal heart rate transition at 80 bpm, Unknown	
33	02-JUL-2015	Electrocardiogram	Intermediate heart,normal conduction times,Unknown	
34	02-JUL-2015	Electrocardiogram	Discreet ST segment depressions V3-V5/II/aVF	
35	03-JUL-2015	Electrocardiogram	Consistent findings with resting ECG from 02-Jul	
36	03-JUL-2015	Electrocardiogram	ST segment depressions in chest leads declining	
37	01-JUN-2015	Haematocrit	39.1 %	47 37
38	13-APR-2015	Haemoglobin	13.1 g/dl	16 12
39	01-JUN-2015	Haemoglobin	13.3 g/dl	16 12
40		Laboratory test	Configuration of NSTEMI, Unknown	
41	01-JUN-2015	Platelet count	207, X10**3/MCL	400 150
42	13-JUL-2015	Platelet count	238, X10**3/MCL	400 150
43	01-JUN-2015	Serum ferritin	708 ng/ml	150 13
44	13-JUL-2015	Serum ferritin	965 ng/ml	150 13
45	01-JUN-2015	White blood cell count	8.7 x 10^3/UL, X10**3/MCL	10 4.3
46	13-JUL-2015	White blood cell count	8.2, X10**3/MCL	10 4.3

13. Relevant Tests

[Coronary angiography] (03-Jul-2015) : (RCX: severe stenosis proximally at the origin, Unknown)
[Coronary angiography] (03-Jul-2015) : (RIVA: 50% stenosis at the origin from main stem, Unknown)
[Resting ECG] (02-Jul-2015) : (Discreet ST segment depressions V3-V5/II/aVF,Unknown)
[Resting ECG] (03-Jul-2015): (Consistent findings with resting ECG from 02-Jul, Unknown
[Resting ECG] (03-Jul-2015): (ST segment depressions in chest leads declining, Unknown)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();

Allergies, tobacco usage and alcohol consumption were not reported. The patient had an allergy to penicillin. The patient was not pregnant and lactating at the time of the report. The patient had nephrosclerosis and abuse of
analgesics which led to renal failure, also reported as chronic renal insufficiency requiring dialysis stage III, diagnosed on 24-Sep-2013. The patient was subjected to hemodialysis and was started on 08-Jan-2014 with an average
frequency of 3 times per week (Monday, Wednesday, Friday). The patient was not treated with Erythropoiesis-Stimulating Agent (ESA) prior to treatment with Retacrit. Medical history included GORD and s/p appendectomy
(1979). Risk factors included arterial hypertension, colon cancer diagnosed on an unknown day in Nov-2012, obesity, hyperlipoproteinaemia, positive family history for cardiovascular

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		disease, ongoing nicotine abuse.
Unknown		(); PRD : (04-Mar-2016) SRD : (05-Mar-2016) Alcohol consumption was not reported. The patient had an allergy to penicillin. The patient was not pregnant and lactating at the time of the report. The patient had nephrosclerosis and abuse of analgesics which led to renal failure, also reported as chronic renal insufficiency requiring dialysis stage III, diagnosed on 24-Sep-2013. The patient was subjected to hemodialysis and was started on 08-Jan-2014 with an average frequency of 3 times per week (Monday, Wednesday, Friday). The patient was not treated with Erythropoiesis-Stimulating Agent (ESA) prior to treatment with Retacrit. Medical history included GORD and s/p appendectomy (1979), hyperlipidemia, ischemic heart disease three-vessel-disease and atrial fibrillation. Risk factors included arterial hypertension, colon cancer diagnosed on an unknown day in Nov-2012, obesity (BMI: 26.81), hyperlipoproteinaemia, positive family history for cardiovascular disease, ongoing nicotine abuse, smoking (packs per day UK).
Unknown to Ongoing	Relevant Med History	Analgesic abuse (Drug abuse);
Unknown to Ongoing	Relevant Med History	Penicillin allergy (Drug hypersensitivity);
Unknown to Ongoing	Relevant Med History	Nephrosclerosis (Nephrosclerosis);
Unknown to Ongoing	Relevant Med History 24-Sep-2013; chronic renal insufficiency stage III	Renal failure (Renal failure);
Unknown	Relevant Med History 1979	Appendectomy (Appendicectomy);
Unknown	Relevant Med History	Gastrooesophageal reflux disease (Gastrooesophageal reflux disease);
Unknown	Relevant Med History Risk Factor	Hypertension arterial (Hypertension);
Unknown	Relevant Med History Risk Factor-Nov-2012	Colon cancer (Colon cancer);
Unknown	Relevant Med History Risk Factor	Hyperlipoproteinaemia (Hyperlipidaemia);
Unknown	Relevant Med History Risk Factor	Obesity (Obesity);
Unknown	Relevant Med History Risk Factor	Nicotine abuse (Tobacco abuse);
Unknown	Relevant Med History Risk Factor	Family history of cardiovascular disorder (Familial risk factor);
Unknown	Relevant Med History Started on 08-Jan-2014	Hemodialysis (Haemodialysis);
Unknown	Relevant Med History Concurrent surgical procedure	Drug-eluting coronary stent placement (Coronary arterial stent insertion);
Unknown 27-Aug-2020 04:52	Relevant Med History	Percutaneous transluminal coronary angioplasty (Coronary

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		angioplasty);
	Concurrent surgical procedure	
Unknown	Past Drug Event	PENICILLIN (PENICILLIN /00000901/); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: Penicillin allergy (Drug hypersensitivity)
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Risk Factor	Smoker (Tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	14	JUL	1934	81 Years	Male	69.00 kg	24	AUG	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cardiac Infarction (type 2) [Myocardial infarction]
Multi organ failure [Multiple organ dysfunction syndrome]
Sepsis [Sepsis]

Case Description: Fatal multi organ failure, fatal sepsis, and cardiac infarction (type 2). Epoetin Zeta. Hospira-sponsored study report received from an investigator (ref: SW005-0028) which refers to a patient. The patient was enrolled in a Post
Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 26-SEP-2015
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 290 IU/kg/ (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low HB (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 13-FEB-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History Diagnosed in 05-Mar-2012	Malignant anorectal neoplasm (Malignant anorectal neoplasm)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3023465

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
11-JAN-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had glomerulonephritis leading to renal failure (first diagnosed on 24-Nov-2006). On 24-Nov-2006, the patient started hemodialysis and receives an average of 4 per week. The patient was previously treated on an unknown date in 2008 with an erythropoiesis-stimulating agent (ESA) epoetin alpha (Eprex, 87 IU/kg/week, route of administration not reported). It was reported that the patient had not experienced any thromboembolic event during treatment with any other ESA. The patient had no previous exposure to other biosimilars. Concomitant medications were not reported. On 13-Feb-2012, the patient started treatment with epoetin zeta (Retacrit, 290 IU/kg/week, 2 dosage /week, subcutaneous; lot number and expiry date were not known) for low HB. On 12-Nov-2013, the patient was enrolled into the study. On 30-Jun-2015, laboratory results showed hemoglobin of 86 G/L (normal values not reported). On 17-Aug-2015, the patient received the last dose of Retacrit prior to the event. On 23-Aug-2015, patient's haemoglobin was at 88 G/L. On 24-Aug-2015 at 4:45, the patient developed cardiac infarction (type 2) and was admitted to hospital. On an unknown date, the patient had sepsis and multi organ failure. Treatment for the event of cardiac infarction was reported as conservative treatment (not specified) due to vascular deformity in stomach; while treatment for the events of sepsis and multi organ failure was not reported. Action taken with the suspect drug in response to the events was not reported.
The patient has recovered from the event of cardiac infarction (type 2) on 28-Aug-2015 and the patient was discharged from the hospital on 10-Sep-2015. On 26-Sep-2015, the patient died. Causes of death were sepsis and multi organ failure. It was not reported if an autopsy was performed. The reporter's opinion of causality between the adverse event cardiac infarction (type 2) and the suspect drug was not related. The reporter stated that the cardiac infarction was due to anemia. It was reported that the patient died due to sepsis and multi organ failure not related to Retacrit. Risk factors included myocardial infarction, atrial fibrillation, hyperlipidaemia, hypertension, cancer (malignant in skin on the right lower eyelid) diagnosed in 05-Mar-2012, and smoking (patient was an ex-smoker). 02-Oct-2015: Additional information was received from the same reporter regarding patient's complete date of birth, date of last dose of Retacrit prior to the event of cardiac infarction; treatment and outcome of the event of cardiac infarction; and hemoglobin results. The type of dialysis the patient was receiving was specified as hemodialysis. The patient had no previous exposure to other biosimilars.
Seriousness criterion for the event of cardiac infarction was changed from medically significant to life threatening and hospitalisation. Hospitalisation dates were also added. Indication of Retacrit was updated to low HB (previously reported as renal anaemia). The reporter's opinion of causality between the event of cardiac infarction (type 2) and Retacrit was provided. This information has been incorporated in the narrative and corresponding data fields. The reporter was unable to provide the following information for indentification and traceability of the biosimilar product Retacrit: batch number and date of expiry.
11-Jan-2016: Additional information was received from the same reporter. Death date of the patient was changed to 26-Sep-2015 (previously 26-Aug-2015). This information was incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not related Although information is limited, it is unlikely for the suspect drug to cause the adverse events given the patient's medical history and multiple risk factors, including myocardial infarction, atrial fibrillation and hypertension. Follow-up: Overall case causality changed to not related given the similar opinion of the reporter. Company causality is as previously stated. Follow-up: No change in previous assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-JUN-2015	Haemoglobin	86 g/l	
2	23-AUG-2015	Haemoglobin	88 g/l	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	290 IU/kg/week, Freq: 2 Week, Interval: 1; Subcutaneous	Low HB (Haemoglobin decreased)	13-FEB-2012 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption not reported. The patient had glomerulonephritis leading to renal failure (first diagnosed on 24-Nov-2006). On 24-Nov-2006, the patient started dialysis and receives an average of 4 per week. The patient was previously treated on an unknown date in 2008 with an erythropoiesis-stimulating agent (ESA) epoetin alpha (Eprex, 87 IU/kg/week, route of administration not reported). It was reported that the patient had not

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		experienced any thromboembolic event during treatment with any other ESA. The patient had no previous exposure to other biosimilars. Race/Ethnicity: Caucasian On 26-Sep-2015, the patient died. Causes of death were sepsis and multi organ failure. It was not reported if an autopsy was performed. Risk factors included myocardial infarction, atrial fibrillation, hyperlipidaemia, hypertension, cancer (malignant in skin on the right lower eyelid) diagnosed in 05-Mar-2012, and smoking (patient was an ex-smoker).
Unknown to Ongoing	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown to Ongoing	Relevant Med History Diagnosed in 24-Nov-2006	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Deformity (Deformity);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
Unknown	Past Drug Event	EPREX (EPREX); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN		JUL	1939	76 Years	Male	71.00 kg	24	JUL	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Embolic cerebral infarction [Embolic cerebral infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This case has been migrated from another database into the current safety database for processing follow-up information.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 42.5 IU/kg/week, 0.5 dosage/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 03-AUG-2012 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Facial palsy (Facial paralysis)
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3023485

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
13-MAY-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report. This is a Non-Interventional Study report from the observational study EPOE-09-11. A 76-year-old male subject started to receive epoetin zeta (RETACRIT) subcutaneously from 03Aug2012 to an unspecified date; and then subcutaneously from 20Nov2015 at 1000 E (as reported) for the treatment of renal anaemia. Medical history included complete central facial palsy on the right side, weakness in the right arm, fistula in left arm, hyperlipidemia, ischaemic heart disease, diabetes mellitus and rectal cancer, diagnosed in 2007. The subject had glomerulonephritis leading to renal failure (first diagnosed on 25-Mar-2009) and was receiving hemodialysis since 06-Aug-2012 with an average of three dialysis per week. The subject had an operation for Warthin's tumor in 2009. Risk factors included coronary heart disease, atrial fibrillation, stroke in 2009, hypertension, many relatives with stroke, Warthin's tumor diagnosed in 22Apr2009, ex-smoker, obesity with BMI of 33.3, PCI on 28-Dec-2015 and ecstatic retroperitoneal lymphadenopathy (RLA). The subject had not been treated with an erythropoietin stimulating agents (ESA) before treatment with Retacrit. Concomitant medications were not reported. On 03Aug2012, the subject began treatment with epoetin zeta (Retacrit, 42.5 IU/Kg/ week, 0.5 dosage per week, frequency also reported as once a week, subcutaneous; batch number not known) for low haemoglobin/ renal anaemia. It was also reported that the therapy start date of the subject was on 22Jul2014. The subject was enrolled in the study on 03Sep2014. On 04May2015 and 05Jun2015, the subject's haemoglobin was 95 g/L and 93 g/L, respectively (normal values not reported). On 24Jul2015, the subject was admitted to the hospital because of an embolic cerebral infarction due to paroxysmal atrial fibrillation. The subject had fistula in left arm, came in with weakness in the right arm and complete central facial palsy on the right side. It was reported that everything was OK when he went to bed at 09:30 PM, but he fell down on the way to the toilet at 04:10 am due to legs unable to bear weight. There were no symptoms of infection, no pain, no dizziness or headaches. Investigations on the same day of 24Jul2015 showed blood pressure of 185 systolic (unit of measurement and normal values not reported); at 06:00 am, the subject's B-hemoglobin was 109 g/L (normal values: 134-170), B-erythrocytes was 3.1 x 10^12/L (normal values: 4.3-5.7), B-thrombocytes at 357 x 10^9/L (normal values: 140-350), B-leucocytes was 13.4 x10^9/L (normal values: 3.5-8.8), P-glucose, non-fasting was 4.8 mmol/L (normal values: 4.2-10.9), P-CRP was less than 5 mg/L (normal value: less than 10), P-potassium was 5.2 mmol/L (normal values: 3.5-4.4), P-calcium was 2.57 mmol/L (normal values: 2.15-2.50), P-albumin was 37 g/L (normal values: 34-45), P-sodium was 139 mmol/L (normal values: 137-145), P-APT-time was short (there may be presence of microalgae in the sample, which can result to short APT time; to rule this out, a new sample must be taken) (normal values: 24-32), P-PK-INR was 1.0 (normal values: 0.8-1.2). On the same day of 24Jul2015, at 06:32:20 am, the subject's head CT showed cochlear implant on the left side that was resulting in the pronounced artifacts. No intracranial hemorrhage. No certain ischemic changes observed in the actual origin but the metal artifacts worsen the assessment significantly on the left side. It also showed lacunar infarction in capsula interna on the left side; 3 mm large highly attenuated punctuate change in right insula of unknown origin and significance, in comparison to the previous examination results due to the absence of thin sections. Investigations performed on 24Jul2015 at 12:30 pm showed P-homocysteine at 156.9 micromol/L (normal value: less than 27), fP-triglycerides was 1.2 microkat/L (normal values: 0.45-2.6), P-LDL-cholesterol was 2.1 mmol/L (normal values: 2.0-5.3), P-cholesterol was 3.7 mmol/L (normal values: 3.9-7.8) and P-HDL-cholesterol was 1.1 mmol/L (normal values: 0.80-2.1). Treatment for the adverse event and action taken with the suspect drug in response to the adverse event were not reported. It was reported that the last dose of Retacrit prior to the event was given on 17Jul2015. The subject was discharged from the hospital on 31Jul2015. Outcome of the event of embolic cerebral infarction was not recovered. The reporter's opinion of causality for the event of embolic cerebral infarction in relation to Retacrit was not reported.

The reporter assessment of the causal relationship of the event with the suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

Follow-up (17Dec2018): New information received from the study nurse included verbatim narrative: There was no TIA attack event reported on this subject.

Amendment: This follow-up report is being submitted to amend previously reported information: Subject age was updated. Information regarding TIA was removed.

Amendment: This follow-up report is being submitted to amend previously reported information: Subject age was updated.

Follow-up (13May2019): New information received by Pfizer from the investigator includes: subject information (age at event onset).

Case Comment: Based on the available information there is not a reasonable possibility that the drug contributed to occurrence of the event. Although the suspect drug can theoretically increase the risk of thromboembolic events, patient has numerous cardiovascular risk factors which far outweigh the potential risk from the suspect drug.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	24-JUL-2015	Activated partial thromboplastin time	Short	32 24
2	24-JUL-2015	Blood albumin	37 g/l	45 34
3	24-JUL-2015	Blood calcium	2.57 mmol/l	2.50

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				2.15
4	24-JUL-2015	Blood cholesterol	3.7 mmol/l	7.8 3.9
5	24-JUL-2015	Blood glucose	4.8 mmol/l	10.9 4.2
6	24-JUL-2015	Blood homocysteine	156.9 umol/l	
7	24-JUL-2015	Blood potassium	5.2 mmol/l	4.4 3.5
8	24-JUL-2015	Blood pressure measurement	185 systolic	
9	24-JUL-2015	Blood sodium	139 mmol/l	145 137
10	24-JUL-2015	Blood triglycerides	1.2 microkat/L Unknown	2.6 0.45
11	24-JUL-2015	C-reactive protein	less than 5 mg/l	10
12	04-MAY-2015	Haemoglobin	95 g/l	
13	05-JUN-2015	Haemoglobin	93 g/l	
14	24-JUL-2015	Haemoglobin	109 g/l	170 134
15	24-JUL-2015	High density lipoprotein	1.1 mmol/l	2.1 0.80
16	24-JUL-2015	International normalised ratio	1.0	1.2 0.8
17	24-JUL-2015	Low density lipoprotein	2.1 mmol/l	5.3 2
18	24-JUL-2015	Platelet count	357 x10 9/l	350 140
19	24-JUL-2015	Red blood cell count	3.1 x10 9/l	5.7 4.3
20	24-JUL-2015	Skull X-ray	in comparison to the previous examination	
21	24-JUL-2015	White blood cell count	13.4 x10 9/l	8.8 3.5

13. Relevant Tests

Head CT (24Jul2015): showed cochlear implant on the left side that was resulting in the pronounced artifacts. No intracranial hemorrhage. No certain ischemic changes observed in the actual origin but the metal artifacts worsen the assessment significantly on the left side. It also showed lacunar infarction in capsula interna on the left side; 3 mm large highly attenuated punctuate change in right insula of unknown origin and significance, in comparison to the previous examination results due to the absence of thin sections.
P-APT-time (24Jul2015): short (there may be presence of microalgae in the sample, which can result to short APT time; to rule this out, a new sample must be taken) (normal values: 24-32)

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	10000 E; Subcutaneous	renal anaemia (Nephrogenic anaemia)	20-NOV-2015 / Unknown;

Mfr. Control Number: 3023485

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
			Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Fistula (Fistula);
Unknown to Ongoing	Relevant Med History glomerulonephritis leading	Glomerulonephritis (Glomerulonephritis); to renal failure
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
2007 to Ongoing	Relevant Med History	Rectal cancer (Rectal cancer);
25-MAR-2009 to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Weakness of arms (Muscular weakness);
Unknown	Family History	Stroke (Cerebrovascular accident);
2009 to 2009	Relevant Med History	Cancer surgery (Cancer surgery);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Retroperitoneal lymphadenopathy (Retroperitoneal lymphadenopathy);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History BMI 33.3	Obesity (Obesity);
2009 to Unknown	Relevant Med History Risk Factor- in 2009	Stroke (Cerebrovascular accident);
22-APR-2009 to 2009	Relevant Med History	Warthin's tumour (Papillary cystadenoma lymphomatosum);
06-AUG-2012 to Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	JUN	1942	73 Years	Male	90.00 kg	16	MAR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombosis of V. fibularis (right side) [Thrombosis]
Thrombosis of V. fibularis posterior (right side) [Thrombosis]

Case Description: Thrombosis of V. fibularis (right side), thrombosis of V. tibialis posterior (right side). Epoetin zeta. Hospira-sponsored study report, received from a physician (ref: Ge-093-0079) which refers to a patient. The patient was enrolled in a Post
Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S025T4; Exp.Dt. 01-NOV-2016}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Drug use for unknown indication (Produ
(Continued on Additional Information Page)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 16-DEC-2013 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) MARCUMAR (PHENPROCOUMON) ; Unknown
#2) METOBETA (METOPROLOL TARTRATE) ; Unknown
#3) AMLODIPIN /00972401/ (AMLODIPINE) ; Unknown
#4) RAMIPRIL (RAMIPRIL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3024253

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included diabetic nephropathy which led to the diagnosis of renal failure in 02-Dec-2011,arterial hypertension, atrial fibrillation, chronic kidney disease stage 5, and was status post bicondylar surface replacement prosthesis of the right knee due to gonarthrosis. The patient had previously been treated with Erythropoiesis- Stimulating Agent (ESA) epoetin alfa (Abseamed). The patient was on dialysis via Cimino shunt on the left (installed in 2012) 3 times per week. Concomitant medications included ramipril 5, amlodipin 5, Metrobeta 200, lecarnidin 20 and Marcumar. On 16-Dec-2013, the patient began treatment with epoetin zeta (Retacrit, 266 IU/Kg/week, 3 dosage per week, subcutaneous; batch number 4V058V4) for renal anaemia. The patient was enrolled in the study on 14-Mar-2014. On 05-Jan-2015 and 23-Feb-2015, the patient's haemoglobin was 12.1 g/DL and 10.6 g/DL, respectively (normal values not reported). On 16-Mar-2015, the patient was admitted due to thrombosis of V. fibularis (right side) also reported as sonographically verified thrombosis of the right fibular vein. Treatment for the adverse event included full heparinisation and marcumarisation with bed rest and compression therapy. The patient was also recommended to present to the vascular surgery outpatient clinic in three months. Action taken with the suspect drug in response to the adverse event was not reported. It was reported that the last dose of Retacrit prior to the event was given on 16-Mar-2015.
The event of thrombosis of V. fibularis (right side) resolved on 20-Mar-2015. End of inpatient treatment was on 20 Mar 2015. On an unknown date, the patient resumed epoetin zeta (batch numbers 4S025T4 and 4U055U4). On 01-Jun-2015 and 13-Jul-2015, the patient's haemoglobin was 9.3 g/DL and 9.3 g/DL, respectively. On 10-Aug-2015, the patient received the last dose of epoetin zeta prior to onset of the second event. On 11-Aug-2015, the patient was hospitalized due to thrombosis of V. tibialis posterior (right side) also reported as sonographically verified thrombosis of the right posterior tibial vein. Treatment for the adverse event included full heparinisation and marcumarisation with bed rest and compression therapy with compression stockings indicated indefinitely and treatment with Marcumar was to be continued for life. End of inpatient treatment was on 21 Aug 2015. The patient was also recommended to present to the vascular surgery outpatient clinic in approximately 6 weeks. Action taken with the suspect drug in response to the adverse event was not reported. Outcome of thrombosis of V. tibialis posterior (right side) resolved on 28-Aug-2015. The reporter's opinion of causality for the events of thrombosis of V. fibularis (right side) and thrombosis of V. tibialis posterior (right side) in relation to epoetin zeta was not assessable. Risk factor included type 2 diabetes without vascular complications. The following information has been requested from the reporter for identification and traceability of the biosimilar product, Retacrit: previous exposure of patient to other biosimilars. 05-Oct-2015: Translation of German text was received.
Medical history of status post bicondylar surface replacement prosthesis of the right knee due to gonarthrosis, atrial fibrillation, and chronic renal disease stage 5 were added. Medical history of hypertension was updated to arterial hypertension. It was reported that the patient had dialysis via Cimino shunt on the left (installed in Jul 2012). It was reported that the patient had a sonographically verified thrombosis of the right posterior tibial vein and sonographically verified thrombosis of the right posterior tibial vein. Sonography results, treatment for the events, and recommendations were provided. End date of inpatient treatment was also provided. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Related Events are possibly related based on medical plausibility. Epoetin can theoretically increase the risk of thrombotic events based on drug mechanism of action. Consider also contributory effects of diabetes in the medical history. Follow-up: No change in previous causality assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	05-JAN-2015	Haemoglobin	12.1 g/dl	
2	23-FEB-2015	Haemoglobin	10.6 g/dl	
3	01-JUN-2015	Haemoglobin	9.3 g/dl	
4	13-JUL-2015	Haemoglobin	9.3 g/dl	
5		Ultrasound scan	Thrombosis of the right posterior tibial vein Un	
6		Ultrasound scan	Thrombosis of the right fibular vein Unknown	

13. Relevant Tests

Sonograph (Date Unknown): Thrombosis of the right posterior tibial vein, Unknown

Mfr. Control Number: 3024253

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S025T4; Exp.Dt. 01-NOV-2016}; Regimen #1	UNK; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4U055U4; Exp.Dt. 01-JAN-2017}; Regimen #2	UNK; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4V058V4; Exp.Dt. 28-FEB-2017}; Regimen #3	UNK; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4S025T4; Exp.Dt. 01-NOV-2016}; Regimen #4	266.6 IU/kg, 3 dosages per week, Freq: 1 week, Interval: 1; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4U055U4; Exp.Dt. 01-JAN-2017}; Regimen #5	266.6 IU/kg, 3 dosages per week, Freq: 1 week, Interval: 1; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4V058V4; Exp.Dt. 28-FEB-2017}; Regimen #6	266.6 IU/kg, 3 dosages per week, Freq: 1 week, Interval: 1; Subcutaneous	Drug use for unknown indication (Product used for unknown indication) Renal anaemia (Nephrogenic anaemia)	16-DEC-2013 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage and alcohol consumption were not reported. Medical history included diabetic nephropathy which led to the diagnosis of renal failure in 02-Dec-2011,arterial hypertension, atrial fibrillation, chronic kidney disease stage 5, and was status post bicondylar surface replacement prosthesis of the right knee due to gonarthrosis. The patient had previously been treated with Erythropoiesis-Stimulating Agent (ESA) epoetin alfa (Abseamed). The patient was on dialysis via Cimino shunt on the left (installed in 2012) 3 times per week. Race/ Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Chronic kidney disease stage 5 (End stage renal disease);
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);
Unknown to Ongoing	Relevant Med History	Gonarthrosis (Osteoarthritis);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History 02-Dec-2011	Renal failure (Renal failure);
Unknown	Relevant Med History	Knee prosthesis insertion (Knee arthroplasty);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown	Relevant Med History	Cimino shunt (Arteriovenous fistula operation);
Unknown	Relevant Med History	Dialysis (Dialysis);
Unknown	Past Drug Event	EPOETIN ALFA (EPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	MAY	1940	74 Years	Female	77.50 kg	04	APR	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: NSTEMI. Epoetin zeta (Retacrit). Hospira-sponsored study report received from an investigator (reference: Ge-093-0056), which refers to a patient. The patient was enrolled in a Hospira-sponsored Post Authorisation Safety Cohort
Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient was not smoking. On an unknown date in 1989, the patient had transient ischemic attack. It was also reported that

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) Freq: 3 Week, Intreval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 02-SEP-2013 / 01-APR-2015

19. THERAPY DURATION
#1) 577 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3033104

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
02-OCT-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

the patient had glomerulonephritis, which led to renal failure diagnosed on an unknown date in May-1997. On an unknown day in May-2001, the patient had hemodialysis (3 dialysis/week). On an unknown day in Jan-2007, prior to Retacrit, the patient was treated with epoetin alfa (Erypo Fs 4000; 645.2 ng/kg/week for the last 3 months, route of administration not reported). The patient had an ongoing ischemic heart disease. The patient was exposed to other erythropetin-stimulating agent (ESA) which included Aranesp (dose illegible, route of administration not reported) from 02-Jul-2008 to 05-May-2010 and haemoglobin count ranged from 10 to 14.7 g/dL; Abseamed (18000 IU/week, route of administration not reported) from 07-May-2010 to 29-Jul-2011 and haemoglobin count ranged from 7.5 to 14.1 g/dL; and Mircera (200 mcg/month, route of administration not reported) from 01-Aug-2011 to 02-Aug-2013 and haemoglobin count ranged from 9.2 to 14.4 g/dL. The patient did not experience any thromboembolic event during these treatments. Concomitant medications not reported. On 02-Sep-2013, the patient was treated with epoetin zeta (Retacrit; 154.8 IU/kg/week, 3 dosages/week, also reported as 1 x per week; lot number not reported) for renal anaemia. On 04-Apr-2015, the patient was diagnosed with NSTEMI and was admitted. Investigations including examinations, laboratory, and diagnostic data, treatment for the events, and action taken with the suspect drugs were not reported. The patient recovered from NSTEMI on 10-Apr-2015 and was discharged. The investigator could not assess the causal relation of the event to the suspect drug. Risk factors included obesity (with BMI of 25.9), coronary heart disease, stroke and hypertension. The following information has been requested from the reporter for the identification and traceability of the biosimilar product Retacrit: previous exposure to other biosimilars.

Case Comment: Overall case causality: Related Event is possibly related to Retacrit based on medical plausibility. The suspect drug is known to theoretically increase the risk of thromboembolic events, but consider also contributory effects of preexistent cardiovascular risk factors in the medical history.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. Patient was not smoking. On an unknown date in 1989, the patient had transient ischemic attack. It was also reported that the patient had glomerulonephritis, which led to renal failure diagnosed on an unknown date in May-1997. On an unknown day in May-2001, the patient had hemodialysis (3 dialysis/week). On an unknown day in Jan-2007, prior to Retacrit, the patient was treated with epoetin alfa (Erypo Fs 4000; 645.2 ng/kg/week for the last 3 months, route of administration not reported). The patient had an ongoing ischemic heart disease. The patient was exposed to other erythropetin-stimulating agent (ESA) which included Aranesp (dose illegible, route of administration not reported) from 02-Jul-2008 to 05-May-2010 and haemoglobin count ranged from 10 to 14.7 g/dL; Abseamed (18000 IU/week, route of administration not reported) from 07-May-2010 to 29-Jul-2011 and haemoglobin count ranged from 7.5 to 14.1 g/dL; and Mircera (200 mcg/month, route of administration not reported) from 01-Aug-2011 to 02-Aug-2013 and haemoglobin count ranged from 9.2 to 14.4 g/dL. The patient did not experience any thromboembolic event during these treatments. Race/ ethinicity: Caucasian
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Obesity (Obesity);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
07-MAY-2010 to 29-JUL-2011	Past Drug Event	ABSEAMED (ABSEAMED); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
02-JUL-2008 to 05-MAY-2010	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
01-JAN-2007 to Unknown	Past Drug Event	ERYPO (ERYPO /00928301/); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
01-AUG-2011 to 02-AUG-2013	Past Drug Event	MIRCERA (MIRCERA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GREECE	01	JUN	1940	74 Years	Male	75.00 kg	28	SEP	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Deterioration of renal function [Renal impairment]
NSTEMI [Acute myocardial infarction]

Case Description: Deterioration of renal function and NSTEMI. Epoetin zeta. Serious Hospira sponsored study report from Greece received from an investigator (reference: Gr-0017-0009), which refers to a 74-year-old Caucasian male patient (height: 172 cm, weight: 75 kg). The patient was enrolled in a Hospira-sponsored study entitled Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 02-AUG-2013 / 21-JUN-2014

19. THERAPY DURATION
#1) 324 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALL OTHER THERAPEUTIC PRODUCTS ; Unknown
#2) AMLOPEN (AMLODIPINE BESILATE) ; Unknown
#3) CARVEDILEN (CARVEDILOL) ; Unknown
#4) CARVEPEN (CARVEDILOL) ; Unknown
#5) CLEXANE (ENOXAPARIN SODIUM) ; Unknown
#6) LASIX /00032601/ (FUROSEMIDE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	BPH (Benign prostatic hyperplasia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2618581

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-NOV-2015

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Patient's medical history included hyperlipidemia, ischemic heart disease, transient ischemic attack, peripheral arterial disease, hypertension, and chronic gastrointestinal disease specified as small bowel bleeding. The patient also had Lcx PCI, RI carotid stent and LE renal artery stent all in 2006; pancreatitis in 2013, CRF, BPH and history of lower gastrointestinal hemorrhages also described as most likely from the small intestine; and Hct of 40% (normal range not reported). The patient had glomerulonephritis which led to renal failure diagnosed in Feb-2009. The patient was not on dialysis. Concomitant medications included Carvedilen (12.5 mg, BD and 125 g, 1 x 2), Procoralan (5 mg, BD; also reported as 5 x 2, also reported as 5 mg, 1 x 2), TTS Nitrong (5 mg, OD, also reported as 5 mg, 1 x 1), Salospir tbs (100 g, 1 x 1, also reported as 100 x 1), Clexane (60 g, 1 x 2) "to today", Torvacard (20 g, 1 x 1(B)); Plavix tbs (75 x 1), Lipitor tbs (40 x 1 and 20 x 1), Carvepen tbs (12.5 x 2), Zantac tbs (dose not reported, x 1), TTS Pancoran (5), Lordin amp (dose not reported, x 2), Lasix tbs (dose not reported, x 1 and 40 mg, 1 x 1), Lonarid tbs (N x 3), Omepracal (1 x 1)(units of measurement not reported), Zylapour (100 mg, 1 x 1), Amlopen (5 mg, 1 x 1), and Zaratral XR (dose not reported, 1 x 1 (his own)) (all routes of administration not reported), all given for unknown indications. The patient was previously treated with an erythropoiesis stimulating agent (ESA) specified as Mircera (methoxy polyethylene glycol-epoetin beta; 333.33 ng/kg/week; route of administration not reported) since May-2011 for an unknown indication. It was reported that the patient did not experience any thromboembolic event during treatment with other ESA. It was also reported that the patient had antiplatelet treatment (unspecified; dose and route of administration not reported) which was interrupted in the last greater than 7 months. On 02-Aug-2013, the patient started treatment with Retacrit (epoetin zeta; 10000 IU per week, dose also reported as 133 IU/kg/week, 1 dosage per week, frequency also reported as Q3, subcutaneous, solution for injection in pre-filled syringe; lot number unknown) for renal anaemia. It was reported that there have been no dose change within 3 months prior to the events. Therapy end date of epoetin zeta was 21-Jun-2014. On 28-Sep-2014, the patient was admitted due to retrosternal distress (recurrent). It was also reported that he was hospitalized due to NSTEMI. On an unknown date, ECG showed SR, Q II, III and avF (pre-existing) and BP was 170/90 mmHg (normal range not reported). It was reported that the patient was asymptomatic throughout his hospitalization. On unknown dates, Trop (hs) were 78, 191, 512 and 873 (units of measurement and normal range not reported). Due to history of hemorrhages from the peptic system, he was administered only with Salospir and LMW heparin (doses and route of administration not reported), and was not put on double antiplatelet treatment. On unknown dates, laboratory tests included hematocrit of 42.3, 39.8, and 39.9, white of 6.63, platelets of 1.19, hemoglobin of 13.1, 12.4, and 12.5, pol of 67.6, lymph of 21.8, mon of 5.6, sugar of 102, urea of 116 and 142, creatinine of 3.0 and 2.88, K of 4.9, Na of 138, SGOT of 21, SGPT of 8, cholesterol of 271, HDL of 38, and trop of 821. For radiological evaluation, CXR showed CI was normal, and no apparent pulmonary infiltrates. Other test showed LV natural dimensions with mildly affected contractility (LVE F approximately 45%), RI was normal, LA was normal, valves were mild MR and mild TR, and periocardium was noted to be free. On 02-Oct-2014, he exited at his own will to undergo a coronary angiography. As exit diagnoses, it was noted that the patient had NSTEMI, CRF, history of hemorrhages from the gastrointestinal system with no hemorrhages in the past months and "panangiopath". There was recommendation for coronary angiopathy. On 03-Oct-2014, the patient was admitted to the cardiology clinic for a planned coronary angiography. On 06-Oct-2014, coronary angiography showed coronary disease and there was a recommendation for angioplasty in LCx. On the same day, a successful angioplasty to LCx with right femoral artery access was done. The damage in LCx was accessed with Choice wire. Then pre-dilatation was performed on the damage with a Sprinter 2.5x15 mm balloon, expansion with a Resolute Integrity 3 x 38 mm stent, and then post-dilatation with an NC Sprinter 3.5 x 15 mm balloon. The final result was very good. It was reported that during coronary angiography and angioplasty there was cardiac arrest, from which the patient was recovered immediately and was hospitalized in the coronary unit where he remained until 08-Oct-2014, when he was moved to a ward in the cardiology unit. Mild troponin and other myocardial enzyme mobility were ascertained from repeated laboratory tests. Full antiplatelet and anticoagulation treatment (unspecified; doses and routes of administration not reported) were administered. Patient's SR on the same day of 06-Oct-2014 was at 70 beats (normal range not reported); "Little R.Q. development II, III, aVF (-) T: V6". Also on the same day, cardio U/S showed EF of 50% (normal range not reported), good dimensions of cardiac activities noted, good mobility was also noted, minor MR and TR noted, and pericardial fat in right ventricle was observed. On an unknown date, there was a progressive decline of the symptoms with a reduction in the myocardial enzymes. Also on an unknown date, the patient mentioned musculoskeletal chest pain secondary to the conduction of CPR. On unknown dates, WBC was 7100 and 11360, PLT was 120000 and 124000, HTC of 41.8 and 34.8, Hb of 13.2 and 11.3, gluc of 107 and 86, urea of 143 and 134, creat of 3.32 and 3.29, K of 4.53 and 4.18, Na of 135 and 138, trop. of 0.36 and 1.14, CPK of 42 and 199, SGOT of 18 and 17, SGPT of 10 and 8 and LDH of 198 and 217 (units of measurement not reported), neut of 65.80% and 77.6%, lymph of 22.10% and 10.7% (all normal ranges not reported). On 13-Oct-2014, the patient exited from the hospital haemodynamically stable, non-symptomatic, with explicit instructions and medication. It was also reported that on 31-Oct-2014, the patient experienced postural hypotension, angina, and shortness of breath/NSTEMI, and was admitted to a hospital. The patient had PCI x 1 LCX. On the same day, the patient was admitted to the nephrology department due to deterioration of renal function due to hypotension vasculopathy. Treatment for the adverse events was not reported. The outcome of the adverse events was unknown at the time of the report. On 18-Nov-2014, the patient was visited. It was reported that the patient had no adverse events of special interest and no other adverse drug reactions during the visit. It was also reported that the patient progressed from pre-dialysis and started dialysis on the same day. Also on the same day of 18-Nov-2014, the patient was withdrawn from the study because he no longer met the inclusion/ exclusion criterion (Patient treated subcutaneously with Retacrit (epoetin zeta) for renal anaemia). The reporter's opinion of causality for the events of deterioration of renal function in relation to epoetin zeta was not related, while not reported in relation to NSTEMI. Risk factors included hyperlipidemia, hypertension, smoking (patient was an ex-smoker for 40 years), recent surgery (PCI x 1 LCX), and vascular anomalies. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure to other biosimilars. 12-Jan-2015: English translation of foreign hospital record was received and additional information were noted. Lcx PCI, RI carotid stent, LE renal artery stent, pancreatitis, CRF, BPH, lower gastrointestinal haemorrhage, Hct of 40% and antiplatelet treatment were added as medical history. The dose of Carvedilen was updated. Salospir, Clexane, Torvacard, Plavix, Lipitor, Carvepen, Zantac, Pancoran, Lordin, Lasix, Lonarid, Zylapour, Omepracal, Amlopen and Zaratral XR were added as concomitant medications. Adverse event onset date for NSTEMI was updated to 28-Sep-2014 (previously reported

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

as 31-Oct-2014). Laboratory and diagnostic tests were provided. These information were incorporated in the narrative and in the corresponding data fields. 17-Feb-2015: Additional information was received from the same reporter. A patient visit was reported with no adverse events of special interest and no other adverse drug reactions during the visit. It was also reported that the patient had progressed from pre-dialysis and started dialysis. Patient's withdrawal from the study was also provided. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible NSTEMI is possibly related to Retacrit. Although patient has numerous cardiovascular risk factors such as hyperlipidemia, smoking and hypertension, he was on Retacrit for almost a year. The suspect drug can theoretically increase the risk of thromboembolic events based on drug mechanism of action. The deterioration of renal function is probably not related and more likely due to natural progression of underlying renal failure. - (11 Nov 2014) Follow-up (21 Jan 2015): Updates noted, but the previous causality assessment for the reported events remain the same. - R. Jacot Follow-up (31 Mar 2015): Overall case causality: Related While there is no change in initial causality assessment, company causality is updated from Possible to Related and Probably not to Not related based on Hospira's binary causality assessment guidelines.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Aspartate aminotransferase	21	
2		Aspartate aminotransferase	10	
3		Aspartate aminotransferase	8	
4		Aspartate aminotransferase	18	
5		Aspartate aminotransferase	17	
6		Blood cholesterol	271	
7		Blood creatine phosphokinase	42	
8		Blood creatine phosphokinase	199	
9		Blood creatinine	3.32	
10		Blood creatinine	2.88	
11		Blood creatinine	3.0	
12		Blood creatinine	3.29	
13		Blood glucose	102	
14		Blood glucose	86	
15		Blood glucose	107	
16		Blood lactate dehydrogenase	196	
17		Blood lactate dehydrogenase	217	
18		Blood potassium	4.9	
19		Blood potassium	4.18	
20		Blood potassium	4.53	

Mfr. Control Number: 2618581

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
21		Blood pressure measurement	170/90 mmHg	
22		Blood sodium	135	
23		Blood sodium	138	
24		Blood urea	142	
25		Blood urea	134	
26		Blood urea	116	
27		Blood urea	143	
28		Chest X-ray		
29		Chest X-ray	CI was normal no apparent pulmonary infiltrates	
30		Ejection fraction	50 %	
31		Electrocardiogram	SR, Q II, III and avF (pre-existing)	
32		Haematocrit	39.9	
33		Haematocrit	42.3	
34		Haematocrit	34.8	
35		Haematocrit	41.8	
36		Haematocrit	39.8	
37		Haemoglobin	12.4	
38		Haemoglobin	12.5	
39		Haemoglobin	13.1	
40		Haemoglobin	11.3	
41		Haemoglobin	13.2	
42		High density lipoprotein	38	
43		Laboratory test	MR and mild TR, and periocardium was free	
44		Laboratory test	Contractility (LVE F approximately 45%)	
45		Laboratory test	LV natural dimensions with mildly affected	
46		Laboratory test	RI normal, LA normal,	

Mfr. Control Number: 2618581

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			valves mild	
47		Lymphocyte count	21.8 %	
48		Lymphocyte count	22.1 %	
49		Lymphocyte count	10.7 %	
50		Monocyte count	5.6	
51		Neutrophil count	65.8 %	
52		Neutrophil count	77.6 %	
53		Platelet count	120000	
54		Platelet count	1.19	
55		Platelet count	124000	
56	06-OCT-2014	Sinus rhythm	70 Beats per minute	
57		Troponin	1.14	
58		Troponin	821	
59		Troponin	191	
60		Troponin	0.36	
61		Troponin	521	
62		Troponin	873	
63		Troponin	78	
64		White blood cell count	11360	
65		White blood cell count	6.63	
66		White blood cell count	7100	
67		White blood cell count	67.6	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	10000 IU, Freq: 1 Week, Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	02-AUG-2013 / 21-JUN-2014; 324 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LIPITOR (ATORVASTATIN CALCIUM) ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#8) LONARID /00154101/ (CAFFEINE, CODEINE PHOSPHATE, PARACETAMOL) ; Unknown

#9) LORDIN /00661201/ (OMEPRAZOLE) ; Unknown

#10) NITRONG (GLYCERYL TRINITRATE) ; Unknown

#11) PANCORAN (GLYCERYL TRINITRATE) ; Unknown

#12) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown

#13) PROCORALAN (IVABRADINE HYDROCHLORIDE) ; Unknown

#14) SALOSPIR (ACETYLSALICYLIC ACID) ; Unknown

#15) TORVACARD (ATORVASTATIN CALCIUM) ; Unknown

#16) ZANTAC (RANITIDINE HYDROCHLORIDE) ; Unknown

#17) ZYLAPOUR (ALLOPURINOL) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. Patient's medical history included hyperlipidemia, ischemic heart disease, transient ischemic attack, peripheral arterial disease, hypertension, and chronic gastrointestinal disease specified as small bowel bleeding. The patient also had RI carotid stent and LE renal artery stent all in 2006; pancreatitis in 2013, CRF, BPH and history of lower gastrointestinal hemorrhages also described as most likely from the small intestine; and Hct of 40% (normal range not reported). The patient had glomerulonephritis which led to renal failure diagnosed in Feb-2009. The patient was not on dialysis.The patient was previously treated with an erythropoiesis stimulating agent (ESA) specified as Mircera (methoxy polyethylene glycol-epoetin beta; 333.33 ng/kg/week; route of administration not reported) since May-2011 for an unknown indication. It was reported that the patient did not experience any thromboembolic event during treatment with other ESA. It was also reported that the patient had antiplatelet treatment (unspecified; dose and route of administration not reported) which was interrupted in the last greater than 7 months. Risk factors included hyperlipidemia, hypertension, smoking (patient was an ex-smoker for 40 years), recent surgery (PCI x 1 LCX), and vascular anomalies. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Cardiac arrest (Cardiac arrest);
Unknown to Ongoing	Relevant Med History	Coronary disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Musculoskeletal chest pain (Musculoskeletal chest pain); Secondary to conduction of CPR
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure); 2009

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Retrosternal discomfort (Chest discomfort);
Unknown to Ongoing	Relevant Med History	Small intestinal bleeding (Small intestinal haemorrhage);
Unknown to Ongoing	Relevant Med History	Transient ischemic attack (Transient ischaemic attack);
Unknown	Relevant Med History Concurrent procedure	Angioplasty (Angioplasty);
Unknown	Relevant Med History	Antiplatelet therapy (Antiplatelet therapy);
Unknown	Relevant Med History	Hematocrit abnormal (Haematocrit abnormal);
Unknown	Relevant Med History 2006	Renal artery stent placement (Renal artery stent placement);
Unknown	Relevant Med History	Lower gastrointestinal hemorrhage (Lower gastrointestinal haemorrhage);
Unknown	Relevant Med History 2013	Pancreatitis (Pancreatitis);
Unknown	Relevant Med History 2006	Carotid artery stent insertion (Carotid artery stent insertion);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History 40 years	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Vascular anomaly (Vascular malformation);
Unknown	Relevant Med History Concurrent procedure	Angiography (Angiogram);
Unknown	Relevant Med History	Resuscitation (Resuscitation);
Unknown	Relevant Med History 18-Nov-2014	Dialysis (Dialysis);
Unknown	Relevant Med History	Angioplasty (Angioplasty);
Unknown	Past Drug Event 333.33 ng/kg/ week	METHOXYPOLYETHYLENE GLYCOL-EPOETIN BETA (METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	18	JAN	1929	86 Years	Male	62.00 kg	25	MAY	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: NSTEMI. Epoetin zeta. Hospira-sponsored study report, received from an Investigator (ref: Ge-115-0102), which refers to a patient. The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of Retacrit
(epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient's medical history included hypertension and ischemic heart disease. The patient had declining kidney leading to renal failure (first diagnosed on 15-

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

15. DAILY DOSE(S)
#1) 32 IU/kg/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 24-FEB-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Kidney failure (Renal failure)
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3079051

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 3079051

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Jan-2014) however did not receive any dialysis. The patient had not been treated with an erythropoietin stimulating agents (ESA) before treatment with Retacrit. Concomitant medications were not reported. On 24-Feb-2014, the patient began treatment with epoetin zeta (Retacrit; 32 IU/Kg/week also reported as 5000 IU, subcutaneous, lot number not reported) for treatment of renal anaemia. It was reported that the patient had a hemoglobin of 8.7 gr/dL (normal values not reported). On 25-May-2015, the patient was hospitalized and experienced NSTEMI. As treatment, the patient underwent PTCA and stent on 25 May 2015. On 03 June 2015, the patient recovered from the adverse event. The reporter's opinion of causality for the event of NSTEMI in relation to Retacrit was not related.

Amendment: This follow-up report is being submitted to amend previously reported information: hospitalization ticked for event as seriousness criteria, hospitalized start date added.

Case Comment: Overall case causality: Related Consider the event to be possibly related. Thromboembolic events are associated with the suspect drug based on its mechanism of action, but consider also contributory effect of pre-existing risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	8.7 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History first diagnosed on 15-Jan-2014	Renal failure (Renal failure);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	07	APR	1955	60 Years	Female	63.00 kg	02	NOV	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
NSTEMI [Acute myocardial infarction]
Thromboembolic events [Embolism]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up CIOMS I or MedWatch report may indicate in the appropriate field that it is an initial report.

Myocardial infarction and thromboembolic events. Epoetin zeta.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-JAN-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATORVASTATIN (ATORVASTATIN) ; Ongoing
#2) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Ongoing
#3) FUROSEMID (FUROSEMIDE) ; Ongoing
#4) SPIRONOLACTON (SPIRONOLACTONE) ; Ongoing
#5) PREDNISON (PREDNISONE) ; Ongoing
#6) URAPIDIL (URAPIDIL) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1984 to Ongoing	Relevant Med History	Lupus erythematosus (Systemic lupus erythematosus)
2003 to Ongoing	Relevant Med History	Lupus nephritis (Lupus nephritis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3082071

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
12-MAY-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Hospira sponsored study report, received from an investigator (reference: Cr-009-0009), which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia.
Medical history included lupus erythematosus and nephropathia luposa which led to renal failure diagnosed in 2003. The patient was on dialysis since 01 Oct 2015, with an average frequency of 3 dialyses per week. The patient was previously treated with an erythropoiesis-stimulating agent (ESA), epoetin beta (Recormon; average total dose of 33.3 IU/kg/week for the last 3 months, route of administration not reported) for an unknown indication.
Concomitant medications were not reported.
On an unknown date in 2014, the patient started to receive epoetin zeta (Retacrit; subcutaneous, dose, frequency and lot number not reported) for renal anaemia. On 28 Oct 2015, the patient signed the informed consent. On 02 Nov 2015, the patient experienced myocardial infarction. On 04 Nov 2015, the patient was enrolled into the study. During the week of entry, the patient received epoetin zeta (Retacrit; 63.3 IU/kg/week, subcutaneous, 1 dosage per week, lot number not reported) for renal anaemia. It was reported that the myocardial infarction occurred 2 days prior to enrollment, and it was reported to be a second MI. It was reported that the patient was hospitalized. On an unknown date, the patient experienced thromboembolic events. The thromboembolic events were noted on a visit dated 28 Apr 2016. Investigations including examinations, laboratory and diagnostic data, and, action taken with epoetin zeta, the treatment for the event, and the outcome of the events were not reported.
The primary investigator did not consider Retacrit to be related to the myocardial infarction.
Causality for the event thromboembolic events was not reported.
Risk factors included coronary heart disease, myocardial infarction, hyperlipidaemia, hypertension, heart failure NYHA stage III, and smoking; patient was an ex-smoker.

28 Apr 2016: Additional information was received from the investigator. Thromboembolic events was added as adverse event and other serious/medically significant was added as seriousness criterion for the said event. This information was incorporated in the narrative and in the corresponding data fields. The reporter was unable to provide the following requested information for traceability and identification of the product Retacrit: Previous exposure to other biosimilars aside from Retacrit and Recormon.

Follow-up (12May2016): New information received from the investigator includes completed targeted questionnaire for Retacrit thromboembolic events. Investigator provided patient's hospital discharge letters. New information reported included:
Patient date of birth updated, type of dialysis reported as haemodialysis as of 01Oct2015, Retacrit data (date of last dose prior to the event reported as 26Oct2015, mean dose 1 63.3 IU/kg/week with haemoglobin 95, mean dose 2: 633 IU/kg/week with haemoglobin 92, there haven't been any dose changes within 3 months prior to the event), other erythropoietin-stimulating agent in the past included Reconmon from 2005 to 2014 at 33,5 IU/kg/week with haemoglobin from 99 to 111, the patient didn't experience any thromboembolic event during treatment with other ESA, risk factors for TE events included smoking; relevant history included ongoing hyperlipidemia (therapy rosuvastatin), ongoing ischaemic heart disease from 2015, ongoing hypertension from 1995, ongoing lupus er. from 1984, ongoing lupus nephropathy from 2003. Event was reported as NSTEMI from 02Nov2015 to 10Nov2015, causality reported as not related, the patient was hospiralized due to event from 02Nov2015 to 10Nov2015, outcome reported as recovered, treatment of the event included: nitrates, heparin, b-blockers, statins, urapidil, diuretic. Concomitant medications included ongoing atorvastatin at 40 mg 1xday for hyperlipidemia, ongoing pantoprazole at 40 mg, 1xday vent (illegible) protection, ongoing furosemide at 40 mg, 2xday as diuretic, ongoing spironolactone atv25 mg, 1xday as diuretic, ongoing prednisone at 10 mg, 1xday for LE, ongoing urapidil at 150 mg daily (frequency 3xday) for hypertension. Laboratory tests included: on 30Sep2015: erythrocytes 3.06x10 12/l, haemoglobin 97 g/l, haematocrit 0.304, leucocytes 12.9x10 9/l, CRP 22 mg/l; on 02Nov2015 at 2:58:08 erythrocytes 3.50, hameoglobin 107 g/l, haematocrit 0.359, leucocytes 14x10 9/l, CK 96 IU/l, cTnI 0.073 ug/l, CRP 8.4 mg/l,; on 02Nov2015 at 12:20:03 cTnI 2.372 ug/l,; on 02Nov2015 at 13:44:50 erythrocytes 3.08 x 10 12/l, haemoglobin 91 g/l, haematocrit 0.290; ECG on 02Nov2015: at admission with a lot of technical difficulties probable sinus rhythm, pulse 129/min, milder difficulties in iv conduction, reduced R wave anteroseptal. Control EEG at discharge: sinus rhythm, pulse 74/min, Q wave in III, AV bloc first degree, milder difficulties in iv conduction, reduced R wave anteroseptal. Coronarography on 06Nov2015: LMCA not affected, LAD without visible angiogenic narrowing, Cx bifurcation stenosis, plaque spreads in OMI proximal segment, RCA occluded in medium segment.
Heart ECHO on 05Nov2015: LA enlarged 59 mm, LVS thickened, combined aortic disorder- moderate to severe AS with PG mean 37 mmHg, AVA 0.5 cm2, AR 2, significant calcification of the mitral annulus, severe MR 4+ with VC 8 mm TR up t0 2+. It was reported that the patient is still in study.

Follow-up attempts are completed. No new information is expected.

Case Comment: Overall case causality: Not related With a prior coronary event two days prior to exposure, and several cardiac risk factors present, consider myocardial infarction to be probably not related to the suspect drug. It also takes usually two weeks after drug administration for significant thrombo-embolic events to take place. Follow-up: Overall case causality: Possible Hospira causality: Not assessable No change in assessment for previous event. New event is unassessable. While labeled, it may potentially be associated with previous preceding event. Cannot provide definitive causation with limited clinical information.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	02-NOV-2015	Blood creatine phosphokinase	96 IU/l	153

Mfr. Control Number: 3082071

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				17
2	30-SEP-2015	C-reactive protein	22 mg/l	5.0
3	02-NOV-2015	C-reactive protein	8.4 mg/l	5.0
4	02-JAN-2015	Haematocrit	0.290	0.470 0.356
5	30-SEP-2015	Haematocrit	0.304	0.470 0.356
6	02-NOV-2015	Haematocrit	0.359	0.470 0.356
7		Haemoglobin	95 g/l	157 119
8		Haemoglobin	92 g/l	157 119
9		Haemoglobin	99-111 g/l	157 119
10	02-JAN-2015	Haemoglobin	91 g/l	157 119
11	30-SEP-2015	Haemoglobin	97 g/l	157 119
12	02-NOV-2015	Haemoglobin	107 g/l	157 119
13	02-JAN-2015	Red blood cell count	3.08 x10 12/l	5.08 3.86
14	30-SEP-2015	Red blood cell count	3.06 x10 12/l	5.08 3.86
15	02-NOV-2015	Red blood cell count	3.50 x10 12/l	5.08 3.86
16	02-JAN-2015	Troponin I	2.372	0.056 0.000
17	02-NOV-2015	Troponin I	0.073	0.056 0.000
18	30-SEP-2015	White blood cell count	12.9 x10 9/l	9.7 3.4
19	02-NOV-2015	White blood cell count	14.0 x10 9/l	9.7 3.4

13. Relevant Tests

cTnI (02Nov2016): 0.073 ug/l and 2.372 ug(l
ECG (02Nov2015): at admission with a lot of technical difficulties probable sinus rhythm, pulse 129/min, milder difficulties in iv conduction, reduced R wave anteroseptal.
Control EEG at discharge: sinus rhythm, pulse 74/min, Q wave in III, AV bloc first degree, milder difficulties in iv conduction, reduced R wave anteroseptal.
Coronarography (06Nov2015): LMCA not affected, LAD without visible angiogenic narrowing, Cx bifurcation stenosis, plaque spreads in OMI proximal segment, RCA occluded in medium segment.
Heart ECHO (05Nov2015): LA enlarged 59 mm, LVS thickened, combined aortic disorder- moderate to severe AS with PG mean 37 mmHg, AVA 0.5 cm2, AR 2, significant calcification of the mitral annulus, severe MR 4+ with VC 8 mm TR up to 2+.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION

Mfr. Control Number: 3082071

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #2	63.3 IU/kg, 1x/week; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	01-NOV-2015 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	633 IU/kg/week; Unknown	Renal anaemia (Nephrogenic anaemia)	Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2015 to Ongoing	Relevant Med History Coronarography	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History	Heart failure NYHA class III (Cardiac failure chronic);
Unknown to Ongoing	Relevant Med History Therapy: Rosuvastatin	Hyperlipidaemia (Hyperlipidaemia);
1995 to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Myocardial infarction (Myocardial infarction);
01-OCT-2015 to Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
01-JAN-2005 to 2014	Past Drug Event	RECORMON (RECORMON /00928301/); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	25	DEC	1953	62 Years	Male	68.00 kg	10	DEC	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cerebral haemorrhage [Cerebral haemorrhage]

Case Description: Cerebral haemorrhage. Epoetin zeta. Hospira-sponsored study report received from a physician (ref: Cr-009-0003) which refers to a patient. The patient was enrolled in a Post Authorisation Safety Cohort Observation (PASCO) of
Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient had chronic pyelonephritis, nephrolithiasis bil., and uropathia obstructiva leading to renal failure (first diagnosed in 2011) and was

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 58.8 IU/kg (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anaemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 26-AUG-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLOPIN /00972401/ (AMLODIPINE) ; Unknown
#2) ANDOL (ACETYLSALICYLIC ACID) ; Unknown
#3) TYREZ (BISOPROLOL FUMARATE) ; Unknown
#4) AMLODIPINE BESILATE W/ PERINDOPRIL ARGININE (AMLODIP
#5) BISOPROLOL (BISOPROLOL) ; 01-JAN-2012 / Unknown
#6) CALCITRIOL (CALCITRIOL) ; 01-JAN-2015 / Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Speech loss (Aphasia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3157227

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
12-FEB-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

receiving hemodialysis since 25-Feb-2015 with an average of three dialysis per week. The patient had hemodialysis on Mondays, Wednesdays and Fridays. The patient has had arterial hypertension and denied having other diseases. The patient had control over anal sphincter, regular appetite; smoked approximately 10 cigarettes a day and the patient took no alcohol. The patient had not received any other erythropoietin stimulating agents (ESA) and did not receive Retacrit before. Concomitant medications included bisoprolol, perindopril-amlodipin, moxonidin, Ca-carbonat, calcitriol, Amlopin 10,0, 5 mg, Tyrez 5 mg and Andol 100 mg. On 26-Aug-2015, the patient began treatment with epoetin zeta (Retacrit; 58.8 IU/Kg/week, one dosage per week, subcutaneous; batch number not reported) for anaemia. The date of last dose of Retacrit prior to the event was on 09-Dec-2015. Investigations performed on 09-Dec-2015, included white blood cells (WBC) at 9.3 x10^9/L (normal values: 3.4-9.7), red blood cells (RBC) at 3.96 x10^12/L (normal values: 4.34-5.72), haemoglobin (HGB) at 115 g/L (normal values: 138-175), haematocrit (HTC) at 0.349 L (normal values: 0.415-0.530), platelets (PLT) at 131 x10^9/L (normal values: 158-424). On 10-Dec-2015, patient experienced cerebral hemorrhage. The patient woke up around 08:30 a.m. without any complaints. After that the patient made coffee and started going to the bathroom and in the bathroom the patient felt weakness of right-sided extremities. The patient wanted to call his children and then noticed slanting of the tongue. He complained of mild headache. The patient denied having nausea, was not vomiting, did not lose consciousness, denied difficulties in eye sight and swallowing. The patient was admitted to neurology due to the clinical manifestations of CVI. The patient was conscious; there are right sided hemiparesis and dysphasia.
Investigations performed on 10-Dec-2015, at 02:22 PM included Na at 143 mmol/L (normal values: 137-146) and K at 5.9 mmol/L (normal values: 3.9-5.1). Investigations performed on 11-Dec-2015, at 01:56 PM included RBC at 4.55 x10^12/ L, HGB at 137 g/L, HTC at 0.419 L , WBC at 7.8 x10^9/L, PLT at 133 x10^9/L, INR 1.01 INR, aPTT 1.00 (normal values: 0.80-1.20) and at 02:30 PM, the tests revealed RBC at 4.29 x10^12/L, HGB at 129 g/L, HTC at 0.382 L, WBC at 8.6 x10^9/L, PLT at 151 x10^9/L, Na at 142 mmol/L and K at 4.2 mmol/L. On the same day, the patient's emergency native brain CT scan revealed regular density of hemispheres of cerebellum and pons. The fourth ventricle was medially located, regular, and pontocerebelar angles were orderly. Supratentorially in the area of basal ganglias there was a visible IC haemorrhage, whose dimensions are 2.94x2.04 cm. In basal ganglias of the both sides but more pronounced on the right side several lacunar ischemic areas were visible. The position of central structures was regular. The width of cerebrospinal fluid spaces was regular. Investigations performed on 12-Dec-2015, at 11:45 AM included RBC at 4.10 x10^12/L, HGB at 124 g/L, HTC at 0.364 L , WBC at 9.3 x10^9/L, PLT at 152 x10^9/L, Na at 135 mmol/L and K at 5.2 mmol/L. On 18-Dec-2015, the patient had a CT scan which revealed partial marginal resorption of intracerebral hematoma of temporal lobe of left hemisphere of forebrain. Other findings corresponded to previous CT scan findings. The patient was referred to a speech therapist. Spontaneous speech of the patient was possible, organized, meaning ful, articulatory mildly insecure. There was buccal oral lingual dyspraxia present. Understanding of other people's speech and instructions was reliable. Repeating was possible and nomination was reliable. Speech therapy was recommended during the treatment at the facility Investigations performed on 21-Dec-2015, at 01:31 PM included Na at 135 mmol/L and K at 4.6 mmol/L. On 22-Dec-2015, the patient started to actively pull right arm and closed right hand with reduced force. The patient did not lift the right leg. The patient sat up with assistance and maintained balance after latency. He did not tolerate being lifted into vertical position. The patient was motivated for physical therapy which should be conducted at home in 15 days 5 times a week: individual exercises of outstretching for all the joints of right extremities, sitting up exercises as well as coordination and balance, exercise of lifting into vertical position if he tolerated it. Exercise should be done in measured portions. On 24-Dec-2015, the patient had an ultrasound-TCD which revealed pronounced asymmetry in the finding of flow velocities between the carotid siphon and middle cerebral arteries, in terms of a mild haemodynamic acceleration on the right side, and mild haemodynamic deceleration in arteries of the left side. Haemodynamic was attenuated in the left posterior cerebral artery. On the same day, the patient had a carotid USG Doppler which revealed morphologic presentation of extracranial part of carotid arteries presents medium wide lumens of both common carotid arteries with diffusely thickened arterial walls. In the terminal segments of both commune carotid arteries marginal, mixed, partly calcified atherosclerotic plaques were visible. Mixed, marginal, partly calcified atherosclerotic plaques were also visible in the area of both carotid sinuses and terminal segments of both internal carotid arteries. The patient was diagnosed with intracerebral haemorrhage in hemisphere, subcortical; spastic hemiplegia, essential (primary) hypertension, chronic renal failure (unspecified) and dysarthria and anarthria. Treatment for the adverse event included bisoprolol (5 mg 1x1), metamizole sodium (dose not reported, PRN), diazepam (dose not reported, PRN), perindopril arginin + amlodipin (10 + 10 mg 1x1), moxonidin (0.2 mg at noon, 0.4 mg in the evening), urapidil (dose not reported, PRN) (routes of administration not reported), saline solution infusions (unspecified, dose not reported) , analgesics, antiemetics, (unspecified, doses and routes of administration not reported). Due to febrile condition and increase of inflammatory parameters antibiotics (unspecified, doses and routes of administration not reported) were included in the therapy. Kinesitherapy was done with the assistance of physical therapist. There was right-sided supranuclear facial paralysis, milder sensomotoric dysphasia, serious paresis of the right arm (the patient lifts the forearm from the surface underneath) as well as serious paresis of the right leg present (the patient moves the leg on the surface) in the follow-up neurologic status before discharge. Haemodialysis was done regularly, the last one was on the day of discharge. The patient was discharged from the hospital on 28-Dec-2015 at 3:00 pm. Action taken with Retacrit in response to the adverse event was not reported.
Outcome of the adverse reaction was persistent however it was also reported that the cessation date of the event was on 28-Dec-2015. The reporter's opinion of causality for the event of cerebral haemorrhage in relation to Retacrit was unlikely. Based on clinical features, course of the treatment and the performed tests the reporter considered that the patient had a typical intracerebelar haemorrhage due to arterial hypertension. Risk factor included hypertension since 2012.
04-Feb-2016: Report created in response to regulatory agency's (HALMED) request. Patient history was also updated in the corresponding data field. 12-Feb-2016: English translation of the Croatian text was received. Clinical presentation,

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

treatment and investigations for the adverse event; details of hospitalization and course of the events were provided. Tobacco usage and alcohol consumption of the patient and alternative etiology of the adverse event were also provided.
Amlopin, Tyrez and Andol were added as concomitant medications. It was reported that the patient had hemodialysis on Mondays, Wednesdays and Fridays and had arterial hypertension and denied having other diseases. It was also reported that the patient had control over anal sphincter and had regular appetite. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Probably Not Event is unlikely due to the suspect drug as patient had preexistent hypertension. Follow up report: No change in previous assessment. Follow-up: No change in previous causality assessment.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-DEC-2015	Activated partial thromboplastin time	1.00 Unknown	1.20 0.80
2	10-DEC-2015	Blood potassium	5.9 mmol/l	5.1 3.9
3	11-DEC-2015	Blood potassium	4.2 mmol/l	5.1 3.9
4	12-DEC-2015	Blood potassium	5.2 mmol/l	5.1 3.9
5	21-DEC-2015	Blood potassium	4.6 mmol/l	5.1 3.9
6	10-DEC-2015	Blood sodium	143 mmol/l	146 137
7	11-DEC-2015	Blood sodium	142 mmol/l	146 137
8	12-DEC-2015	Blood sodium	135 mmol/l	146 137
9	21-DEC-2015	Blood sodium	135 mmol/l	146 137
10	18-DEC-2015	Computerised tomogram	Partial marginal resorption of intracerebral Unkno	
11	18-DEC-2015	Computerised tomogram	hematoma of temporal lobe Unknown	
12	18-DEC-2015	Computerised tomogram	of left hemisphere of forebrain Unknown	
13	11-DEC-2015	Computerised tomogram head	Regular density of hemispheres Unknown	
14	11-DEC-2015	Computerised tomogram head	and pontocerebelar angles were orderly Unknown	
15	11-DEC-2015	Computerised tomogram head	whose dimensions are 2.94x2.04 cm Unknown	
16	11-DEC-2015	Computerised tomogram head	there was a visible IC haemorrhage Unknown	
17	11-DEC-2015	Computerised tomogram head	of cerebellum and pons Unknown	
18	11-DEC-2015	Computerised tomogram head	pronounced on the right side several lacunar Unkn	
19	11-DEC-2015	Computerised tomogram head	ischemic areas were visible Unknown	
20	11-DEC-2015	Computerised tomogram head	Width of cerebrospinal fluid spaces was regular U	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
21	11-DEC-2015	Computerised tomogram head	Supratentorially in the area of basal ganglias Un	
22	11-DEC-2015	Computerised tomogram head	Position of central structures was regular Unknow	
23	11-DEC-2015	Computerised tomogram head	In basal ganglias of the both sides but more Unkn	
24	11-DEC-2015	Computerised tomogram head	Fourth ventricle was medially located, regular Unk	
25	09-DEC-2015	Haematocrit	0.349 l	0.530 0.415
26	11-DEC-2015	Haematocrit	0.382 l	0.530 0.415
27	11-DEC-2015	Haematocrit	0.419 l	0.530 0.415
28	12-DEC-2015	Haematocrit	0.364 l	0.530 0.415
29	09-DEC-2015	Haemoglobin	115 g/l	175 138
30	11-DEC-2015	Haemoglobin	129 g/l	175 138
31	11-DEC-2015	Haemoglobin	137 g/l	175 138
32	12-DEC-2015	Haemoglobin	124 g/l	175 138
33	11-DEC-2015	International normalised ratio	1.01 INR Unknown	
34	09-DEC-2015	Platelet count	131 x10 9/l	424 158
35	11-DEC-2015	Platelet count	151 x10 9/l	424 158
36	11-DEC-2015	Platelet count	133 x10 9/l	424 158
37	12-DEC-2015	Platelet count	152 x10 9/l	424 158
38	09-DEC-2015	Red blood cell count	3.96 x10 12/l	5.72 4.34
39	11-DEC-2015	Red blood cell count	4.29 x10 12/l	5.72 4.34
40	11-DEC-2015	Red blood cell count	4.55 x10 12/l	5.72 4.34
41	12-DEC-2015	Red blood cell count	4.10 x10 12/l	5.72 4.34
42	24-DEC-2015	Ultrasound Doppler	marginal, mixed, partly calcified Unknown	
43	24-DEC-2015	Ultrasound Doppler	diffusely thickened arterial walls Unknown	
44	24-DEC-2015	Ultrasound Doppler	carotid sinuses and terminal segments Unknown	
45	24-DEC-2015	Ultrasound Doppler	atherosclerotic plaques were visible Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
46	24-DEC-2015	Ultrasound Doppler	Mixed, marginal, partly calcified atherosclerotic	
47	24-DEC-2015	Ultrasound Doppler	part of carotid arteries presents medium Unknown	
48	24-DEC-2015	Ultrasound Doppler	Terminal segments both commune carotid arteries U	
49	24-DEC-2015	Ultrasound Doppler	of both internal carotid arteries Unknown	
50	24-DEC-2015	Ultrasound Doppler	wide lumens of both common carotid arteries with	
51	24-DEC-2015	Ultrasound Doppler	plaques were also visible in the area of both Unkn	
52	24-DEC-2015	Ultrasound Doppler	Morphologic presentation of extracranial Unknown	
53	24-DEC-2015	Ultrasound skull	Haemodynamic was attenuated in the left Unknown	
54	24-DEC-2015	Ultrasound skull	haemodynamic deceleration in arteries Unknown	
55	24-DEC-2015	Ultrasound skull	of the left side Unknown	
56	24-DEC-2015	Ultrasound skull	Pronounced asymmetry in the finding of flow Unknow	
57	24-DEC-2015	Ultrasound skull	acceleration on the right side, and mild Unknown	
58	24-DEC-2015	Ultrasound skull	posterior cerebral artery Unknown	
59	24-DEC-2015	Ultrasound skull	cerebral arteries,in terms of a mild haemodynamic	
60	24-DEC-2015	Ultrasound skull	velocities between the carotid siphon and middle U	
61	09-DEC-2015	White blood cell count	9.3 x10 9/l	9.7 3.4
62	11-DEC-2015	White blood cell count	7.8 x10 9/l	9.7 3.4
63	11-DEC-2015	White blood cell count	8.6 x10 9/l	9.7 3.4
64	12-DEC-2015	White blood cell count	9.3 x10 9/l	9.7 3.4

13. Relevant Tests

Carotid USG Doppler (24 Dec2015): Mixed, marginal, partly calcified atherosclerotic Unknown
Carotid USG Doppler (24 Dec2015): plaques were also visible in the area of both Unknown
Carotid USG Doppler (24 Dec2015): Terminal segments both commune carotid arteries Unknown
Carotid USG Doppler (24 Dec2015): wide lumens of both common carotid arteries with Unknown
CT scan (18 Dec2015): Partial marginal resorption of intracerebral Unknown
Native brain CT scan (11 Dec2015): In basal ganglias of the both sides but more Unknown
Native brain CT scan (11 Dec2015): Fourth ventricle was medially located, regular Unknown

ADDITIONAL INFORMATION

13. Relevant Tests

Native brain CT scan (11 Dec2015): Position of central structures was regular Unknown
Native brain CT scan (11 Dec2015): pronounced on the right side several lacunar Unknown
Native brain CT scan (11 Dec2015): Supratentorially in the area of basal ganglias Unknown
Native brain CT scan (11 Dec2015): Width of cerebrospinal fluid spaces was regular Unknown
Ultrasound-TCD (24 Dec2015): cerebral arteries,in terms of a mild haemodynamic Unknown
Ultrasound-TCD (24 Dec2015): Pronounced asymmetry in the finding of flow Unknown
Ultrasound-TCD (24 Dec2015): velocities between the carotid siphon and middle Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	58.8 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Anaemia (Anaemia)	26-AUG-2015 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) AMLODIPINE BESILATE W/ PERINDOPRIL ARGININE (AMLODIPINE BESILATE, PERINDOPRIL ARGININE) ; 01-JAN-2012 / Unknown

#7) CALCIUM CARBONATE (CALCIUM CARBONATE) ; 01-JAN-2015 / Unknown

#8) MOXONIDIN (MOXONIDINE) ; 01-JAN-2012 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies were not reported. The patient had chronic pyelonephritis, nephrolithiasis bil., and uropathia obstructiva leading to renal failure (first diagnosed in 2011) and was receiving hemodialysis since 25-Feb-2015 with an average of three dialysis per week. The patient had hemodialysis on Mondays, Wednesdays and Fridays. The patient has had arterial hypertension and denied having other diseases. The patient had control over anal sphincter, regular appetite; smoked approximately 10 cigarettes a day and the patient took no alcohol. The patient had not received any other erythropoietin stimulating agents (ESA) and did not receive Retacrit before. Race/Ethnicity: Caucasian
Unknown to Ongoing	Relevant Med History	Chronic pyelonephritis (Pyelonephritis chronic);
Unknown to Ongoing	Relevant Med History	Dysarthria (Dysarthria);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism);
Unknown to Ongoing	Relevant Med History	Hyperphosphatemia (Hyperphosphataemia);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Spastic hemiplegia (Hemiplegia);
Unknown	Relevant Med History	Nephrolithiasis (Nephrolithiasis);
Unknown	Relevant Med History	Uropathy obstructive (Urinary tract obstruction);
Unknown	Relevant Med History	Hypertension arterial (Hypertension); Risk Factor:since 2012; Alternative cause
Unknown	Relevant Med History	Smoker (Tobacco user);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Risk Factor	
Unknown	Relevant Med History Concurrent procedure	Haemodialysis (Haemodialysis);
Unknown	Relevant Med History	Abstains from alcohol (Abstains from alcohol);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	10	JUL	1982	33 Years	Male	Unk	27	FEB	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute cardiovascular insufficiency [Cardiovascular insufficiency]
Acute respiratory failure [Acute respiratory failure]
Left femuropopliteal phlebothrombosis [Venous thrombosis]

Case Description: Fatal acute cardiovascular insufficiency, fatal acute respiratory failure and left femuropopliteal phlebothrombosis. Epoetin zeta.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 27-FEB-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 88 IU/kg, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-AUG-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CHLOPHAZOLIN (CLONIDINE HYDROCHLORIDE) ; 01-MAY-2013 / 27-FEB-2016

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History Dec-2012	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3194650

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
29-FEB-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Hospira-sponsored study report received from an investigator (ref: Bg-014-0026), which refers to a patient. The patient was enrolled in the Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. Patient's medical history included glomerulonephritis which led to chronic renal failure grade IV diagnosed on an unknown date in Dec-2012; secondary anaemia; long-term ambulatory peritoneal dialysis; and renal osteodystrophy. On 23-May-2013, the patient had her first dialysis, with an average of 4 dialysis per week). The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medication included chlophazolin. On an unknown day in Aug-2014, the patient began treatment with epoetin zeta (Retacrit; 88 IU/kg/week, 2 dosages/week, subcutaneous; lot number unknown) for renal anaemia. The patient was enrolled in the study on 04-Feb-2016. On an unknown date, the patient developed acute cardiovascular insufficiency, acute respiratory failure and left femuropopliteal phlebothrombosis. Date of lase dose prior to the event was 22-Feb-2016. On 24-Feb-2016, it was reported that the patient was transferred from the department of nephrology and dialysis to the department of surgery because of pain, heaviness, swelling and tension in the left leg, which lasted for 5-6 days. Clinical findings with local, somatic and specialised status included poor general condition, skin and visible mucosa was pale, tongue was wet, but not furred, lungs: weakened vesicular breathing with added singular wet wheezing; heart: rhythmic heart activity, systolic murmur at the apex; abdomen: at the level of the thorax, with diffuse pain; peristaltics normal; local status: tension in subcutaneous veins, subfascial edema of the shank, and a difference in volume between the two shanks of 5-6 cm; and necrotic areas in the shank. On the same day of 24-Feb-2016 at 05:05:36 pm, laboratory test results included total protein of 63 g/l (normal range: 58-80), albumin of 14.2 g/l (normal range: 34-48), ASAT of 29 U/l (normal range: 2-40), ALAT of 10 U/l (normal range: 2-41), urea of 24.7 mmol/l (normal range: 1.7-8.3), creatinine of 861 mcmol/l, uric acid 511.8 mcmol/l, GGT of 209 U/l (normal range: 11-50), AF of 312 U/l (normal range: 0-94), cholesterol of 3.45 mmol/l (normal range: 2.9-5.16), triglycerides of 2.76 mmol/l (normal range: 0.45-1.7), total calcium of 2 (normal range: 2.1-2.6), CRP (C-reactive protein) of 290 U/l, phosphorus of 1.73 mmol/l (upper limit: 7.77), serum iron of 7.2 mcmol/l, TIBC of 21.9 mcmol/l (normal range: 52.1-77), total bilirubin of 23 mcmol/l, glucose of 6.32 mmol/l (normal range: 2.9-6.3), sodium of 132 (normal range: 135-155), potassium of 4.8 mmol/l (normal range: 3.5-5.5), chloride of 82 (normal range: 95-106). On 25-Feb-2016 at 01:14:32 pm, additional laboratory test results showed leukocytes of 48.4 G/l, erythrocytes of 2.5 10/00 (normal range: 4.6-6.2), hemoglobin of 81 g/l (normal range: 140-180), hematocrit of 0.23% (normal range: 0.40-0.54), MCV of 92 Fl (normal range: 79- 97), MCH of 32 Pg (normal range: 26-33.5), MCHC of 348 g/l (normal range: 314-370), ESR of 120 mm/h (normal range: 2-12), and platelets of 369 g/l (150-450). Additional laboratory and diagnostic tests included prothrombin time of 51%, INR of 1.82, fibrinogen of 7.2 (unspecified units of measure), ECG which revealed syn rhythm, isch, and repolarisation changes; ultrasound showed diffuse liver process and bilateral nephrosclerosis; X-ray revealed pulmonary congestion, heart shadow enlarged on the left; and doppler sonography showed occlusion of the vena poplitea sinistra while vena femoralis com, et vena iliaca sin were patent. On the 26-Feb-2016, about 10-11 am, the patient in an extremely severe general status, not adequate, and barely responsive, was transferred to the department of nephrology and dialysis for dialysis. Action taken with with the suspect drug was not reported. Treatment for the events was reported as Tercef 2 x 1 g, heparin 4 x 5000 U, and physiological saline solution 100 ml (routes of administration not reported). Outcome of the event of left femuropopliteal phlebothrombosis was not reported. The patient died on 27-Feb-2016 at 07:30 am. Causes of death was reported as cardiopulmonary insufficiency and acute respiratory failure. It was reported that autopsy was not performed. The reporter's opinion of causality between the event thrombophlebitis and the suspect drug was unlikely, while it was not reported for the events fatal acute cardiovascular insufficiency and fatal acute respiratory failur. Risk factor included symptomatic hypertension, also reported as arterial hypertension second degree. 09-Mar-2016: Additional information was received from the investigator. Death date was confirmed to be on 27-Feb-2016 (previously 26-Feb-2016). It was reported that no autopsy was performed. It was also reported that the patient was hospitalized on 24-Feb-2016 due to thrombophlebiitis. Outcome of thrombophlebitis was updated to not reported (previously fatal). Laboratory data was also added. This information was incorporated in the narrative and corresponding data fields. 19-Mar-2016: Translation of discharge summary was received. Adverse event terms were updated from fatal cardiopulmonary insufficiency and thrombophlebitis to Fatal acute cardiovascular insufficiency, fatal acute respiratory failure and left femuropopliteal phlebothrombosis. Acute respiratory failure was added as a cause of death. Time of death was provided. Secondary anaemia, long-term ambulatory peritoneal dialysis, and renal osteodystrophy were added as medical history. On 24-Feb-2016, it was reported that the patient was transferred from the department of nephrology and dialysis to the department of surgery because of pain, heaviness, swelling and tension in the left leg, which lasted for 5-6 days. Clinical findings were provided. Additional laboratory and diagnostic tests (prothrombin time, INR, fibrinogen, ECG, ultrasound, X-ray, and Doppler sonography) were provided. Treatment for the events was provided. The risk factor hypertension was further described as symptomatic hypertension, also reported as arterial hypertension, second degree. This information has been incorporated in the narrative and corresponding data field.

Case Comment: Overall case causality: Related Although information is limited at this time, causality is being conservatively assessed as possibly related based on medical plausibility as the suspect drug can theoretically increase the risk of thromboembolic events. Follow-up: No change in previous assessment. Follow-up: The added adverse event of respiratory failure is also possibly related as this is a potential sequela from the previously reported thromboembolic event, but consider also contributory effects from patient's multiple comorbidities (renal failure, hypertension and secondary anemia).

Mfr. Control Number: 3194650

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	24-FEB-2016	Alanine aminotransferase	10 IU/l	41 2
2	24-FEB-2016	Aspartate aminotransferase	29 IU/l	40 2
3	24-FEB-2016	Blood albumin	Albumin g/l	48 34
4	24-FEB-2016	Blood alkaline phosphatase	312 IU/l	94 0
5	24-FEB-2016	Blood bilirubin	23 MCMOL/L	
6	24-FEB-2016	Blood calcium	2 mmol/l	2.6 2.1
7	24-FEB-2016	Blood chloride	82 mmo/l	106 95
8	24-FEB-2016	Blood cholesterol	3.45	5.16 2.9
9	24-FEB-2016	Blood creatinine	861 MCMOL/L	
10		Blood fibrinogen	7.2 Unknown	
11	24-FEB-2016	Blood glucose	6.32 mmol/l	6.3 2.9
12	24-FEB-2016	Blood iron	7.2 MCMOL/L	
13	24-FEB-2016	Blood phosphorus	1.73 mmol/l	7.77
14	24-FEB-2016	Blood potassium	4.8 mmol/l	
15	24-FEB-2016	Blood sodium	132 mmol/l	155 135
16	24-FEB-2016	Blood triglycerides	2.76 mmol/l	1.7 0.45
17	24-FEB-2016	Blood urea	24.7 mmol/l	8.3 1.7
18	24-FEB-2016	Blood uric acid	511.8 MCMOL/L	
19	24-FEB-2016	C-reactive protein	290 IU/l	
20		Electrocardiogram	Syn rhythm, isch, and repolarisationchanges Unknow	
21	24-FEB-2016	Gamma-glutamyltransferase	209 IU/l	50 11
22	25-FEB-2016	Haematocrit	0.23 %	0.54 0.40
23	25-FEB-2016	Haemoglobin	81 g/l	180 140
24		International normalised ratio	1.82 Unknown	
25	24-FEB-2016	Iron binding capacity total	21.9 MCMOL/L	
26	25-FEB-2016	Mean cell haemoglobin	32 pg	33.5 26
27	25-FEB-2016	Mean cell haemoglobin	348 g/l	370

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		concentration		314
28	25-FEB-2016	Mean cell volume	92 FL	
29	25-FEB-2016	Platelet count	369 g/l	450 150
30	24-FEB-2016	Protein total	63 g/l	80 58
31		Prothrombin time	51 %	
32	25-FEB-2016	Red blood cell count	2.5 10/00 Unknown	6.2 4.6
33	25-FEB-2016	Red blood cell sedimentation rate	120 mm/h Unknown	12 2
34		Ultrasound Doppler	Patent vena femoralis com, et venailiaca sin Unkno	
35		Ultrasound Doppler	Occlusion of the vena poplitea sinistra Unknown	
36	25-FEB-2016	White blood cell count	48.4 g/l	
37		X-ray	Pulmonary congestion Unknown	
38		X-ray	Heart shadow enlarged on the left Unknown	

13. Relevant Tests

Doppler sonography (UNKNOWN DATE): Patent vena femoralis com, et venailiaca sin Unknown
Electrocardiogram (UNKNOWN DATE): Syn rhythm, isch, and repolarisationchanges Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	88 IU/kg, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	01-AUG-2014 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, tobacco usage, and alcohol consumption were not reported. Patient's medical history included glomerulonephritis which led to chronic renal failure grade IV diagnosed on an unknown date in Dec-2012; secondary anaemia; long-term ambulatory peritoneal dialysis; and renal osteodystrophy. On 23-May-2013, the patient had her first dialysis, with an average of 4 dialysis per week). The patient was not treated with an erythropoiesisstimulating agent (ESA) before treatment with Retacrit. Risk factor included symptomatic hypertension, also reported as arterial hypertension second degree. Race/Ethnicity: Caucasian The patient died on 27-Feb-2016 at 07:30 am. Causes of death were reported as cardiopulmonary insufficiency and acute respiratory failure. It was reported that autopsy was not performed.
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis);
Unknown	Relevant Med History	Renal osteodystrophy (Chronic kidney disease-mineral and bone

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		disorder);
Unknown	Relevant Med History	Secondary anaemia (Anaemia);
Unknown	Relevant Med History Risk Factor-Second degree	Hypertension arterial (Hypertension);
Unknown	Relevant Med History 4 dialysis/ week	Peritoneal dialysis (Peritoneal dialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	OCT	1932	83 Years	Male	71.00 kg	09	FEB	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Thrombosis of V.femoralis communis [Thrombosis]
Death [Death]
NSTEMI [Acute myocardial infarction]

Case Description: Death, thrombosis of V. femoralis communis and NSTEMI. Epoetin zeta.
Hospira-sponsored study report received from an investigator (ref: GE-093-0138) which refers to a patient.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 06-APR-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

15. DAILY DOSE(S)
#1) 169 IU/kg/week, 3 dosage/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 08-MAY-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3194713

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia. Patient had a history of smoking (start and stop dates were unknown). Medical history included coronary heart disease, hypertensive nephropathy which led to renal failure diagnosed in Nov 2014. On 19-Jun-2015, the patient had his first haemodialysis, with an average of 3 haemodialysis per week. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Concomitant medications were not reported. On 08-May-2015 (also reported as 27 Jun 2015), the patient began treatment with epoetin zeta (Retacrit; lot number not available, 169 IU/kg/week, 3 dosage/week, subcutaneous) for renal anaemia. On 08-Jan-2016, there has been a dose change to 24000 IU per week. Haemoglobin prior to dose change was 9.6 G/DL. Haemoglobin after dose change was 8.9 G/DL. On 27-Jan-2016, at 24000 IU per week, haemoglobin was 8.9 G/DL. On 09-Feb-2016, the patient developed thrombosis of V. femoralis communis. On 09-Feb-2016, Quick was 97.0% (reference value: 70-130), INR was 1.02 (reference value: 0.86-1), aPTT was 25.1 sec (reference value: 25.1-36) and fibrinogen was greater than 700 mg/dl (reference value: 276 – 471). Treatment for the event included Marcumar (dose depending on INR, route of administration not reported). On 11-Feb-2016, Quick was 88%, INR was 1.09 and PTT was 29.2 sec (reference value: 26.1- 36.6). On 16-Feb-2016, at 24000 IU per week, haemoglobin was 9.3 G/DL. On 08-Mar-2016, patient experienced NSTEMI. Action taken with the suspect drug was not reported. The event thrombosis was still ongoing and the outcome of NSTEMI was unknown. The patient died on 06 Apr 2016. Cause of death was unknown. It was not reported if autopsy was performed. The reporter's opinion of causality between the event thrombosis and the suspect drug was not assessable while it was unknown for NSTEMI and not reported for death. Risk factors included ischaemic heart disease, hypertension, and prostate cancer since 09-Dec-2014. 21 Apr 2016: Additional information was received from the same reporter. Death and NSTEMI were added as adverse events. Patient had a history of smoking (start and stop dates were unknown). Coronary heart disease was added as medical history. On 08-Jan-2016, there has been a dose change to 24000 IU per week. Haemoglobin prior to dose change was 9.6 G/DL. Haemoglobin after dose change was 8.9 G/DL. On 27-Jan-2016, at 24000 IU per week, haemoglobin was 8.9 G/DL. On 16-Feb-2016, at 24000 IU per week, haemoglobin was 9.3 G/DL. Patient's weight was update to 71 kg also reported as 65 kg (previously reported as 66 kg). The reporter was not able to provide the following information for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Related Event is possibly related based on medical plausibility. The suspect drug can theoretically increase the risk of thromboembolic events based on mechanism of action, but consider also contributory effects of preexistent cardiovascular risk factors. Follow-up: Thrombosis of V. femoralis communis and NSTEMI with the same causality. Death is unassessable without objective clinical event details, including post-mortem findings.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09-FEB-2016	Activated partial thromboplastin time	25.1 seconds	36 25.1
2	11-FEB-2016	Activated partial thromboplastin time	29.2 seconds	36.6 26.1
3	09-FEB-2016	Blood fibrinogen	Greater than 700 mg/dl	471 276
4		Haemoglobin	9.6 g/dl	
5		Haemoglobin	8.9 g/dl	
6	27-JAN-2016	Haemoglobin	8.9 g/dl	
7	16-FEB-2016	Haemoglobin	9.3 g/dl	
8	09-FEB-2016	International normalised ratio	1.02 Unknown	1 0.86
9	11-FEB-2016	International normalised ratio	1.09 Unknown	1 0.86
10	09-FEB-2016	Prothrombin time	97.0 %	130 70
11	11-FEB-2016	Prothrombin time	88 %	130

Mfr. Control Number: 3194713

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				70

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		();
		Allergies and alcohol consumption were not reported. Patient had a history of smoking (start and stop dates were unknown). Medical history included coronary heart disease, hypertensive nephropathy which led to renal failure diagnosed in Nov 2014. On 19-Jun-2015, the patient had his first haemodialysis, with an average of 3 haemodialysis per week. The patient was not treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit. Risk factors included ischaemic heart disease, hypertension, and prostate cancer since 09-Dec-2014. Race/Ethnicity: Caucasian.
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History Diagnosed in Nov 2014	Renal failure (Renal failure);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Risk Factor - since 09-Dec-2014	Prostate cancer (Prostate cancer);
Unknown	Relevant Med History	Smoker (Tobacco user);
Unknown	Relevant Med History average of 3 haemodialysis per week	Haemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	MAR	1940	76 Years	Male	74.50 kg	03	MAR	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Cardiac infarction [Myocardial infarction]

Case Description: Cardiac Infarction. Epoetin zeta. Hospira sponsored study report received from an Investigator (reference: Ge-094-0027), which refers to a patient. The patient was enrolled in a Hospira-Sponsored Post Authorisation Safety Cohort
Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia. The patient was an ex-smoker.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 55.5 IU/kg (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 14-SEP-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3234236

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-APR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Patient's medical history included diabetic nephropathy which led to renal failure diagnosed in Aug-2006. It was reported that the patient had his first hemodialysis in Aug-2014 with an average frequency of 3 dialysis per week. In 2015, the patient received an erythropoetin-stimulating agent (ESA) treatment epoetin theta (Eporatio; 55.5 IU/kg/week) for the last 3 months, before treatment with Retacrit. The patient had not received Retacrit prior the study. Concomitant medications were not reported. On 14-Sep-2015, the patient signed the informed consent and began treatment with epoetin zeta (Retacrit; lot number not reported, 55.5 IU/kg/week, 2 dosages per week, subcutaneous) for renal anaemia. On 29 Feb 2016, the patient received the last dose of epoetin zeta (3 dosages per week, dose not reported) prior to the event. On 03 Mar 2016, the patient had cardiac infarction, described to be a thromboembolic event. It was reported that the patient was admitted to hospital because of the adverse reaction; however, hospitalization start date was reported as 29 Feb 2016. It was reported that hospitalization was ongoing at the time of report. Investigations including examinations, laboratory and diagnostic data, treatment and action taken with the suspect drug were not reported. The patient recovered from the event on 04 Mar 2016. The reporter's opinion of causality between the event and the suspect drug was not related. Risk factors included coronary artery disease, peripheral arterial disease, stroke, hyperlipidaemia, hypertension, diabetes type 2 with diabetic complications and smoking. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: batch number, date of expiry, previous exposure of patient to other biosimilars. 14-Apr-2016: Additional information was received from the same reporter. The event cardiac infarction was described to be a thromboembolic event. This information has been incorporated in the narrative. 22-Apr-2016: Additional information was received from the same reporter. The reporter's opinion of causality between the event and the suspect drug was provided as not related. This information has been incorporated in the narrative and in the corresponding data fields.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable While labeled, cannot provide definitive causation without objective clinical event details and further information on specific pathology of cardiac infarction (thromboembolic vs differential causes). Follow-up: Overall case causality: Related Possibly related by way of temporal relationship and biologic plausibility for this labeled event, but consider also reported patient risk factors. Follow-up: Overall case causality: Not related Reporter causality is noted. Consider cardiac infarction as more likely due to CAD, PAD, hyperlipidemia and other predisposing and pre-existing CV risk factors.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	55.5 IU/kg/week, Freq: 2 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	14-SEP-2015 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. The patient was an ex-smoker. Patient's medical history included diabetic nephropathy which led to renal failure diagnosed in Aug-2006. It was reported that the patient had his first hemodialysis in Aug-2014 with an average frequency of 3 dialysis per week. In 2015, the patient received an erythropoetin-stimulating agent (ESA) treatment epoetin theta (Eporatio; 55.5 IU/kg/week) for the last 3 months, before treatment with Retacrit. The patient had not received Retacrit prior the study. Race/Ethnicity: Caucasian. Risk factors included coronary artery disease, peripheral arterial disease, stroke, hyperlipidaemia, hypertension, diabetes type 2 with diabetic complications and smoking.
Unknown to Ongoing	Relevant Med History Aug-2006	Renal failure (Renal failure);
Unknown	Relevant Med History Risk Factor-Coronary artery disease	Coronary artery disease (Coronary artery disease);
Unknown	Relevant Med History Risk Factor-Diabetic vascular disorder	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);

Mfr. Control Number: 3234236

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	Risk Factor-Type 2 diabetes mellitus	
Unknown	Relevant Med History Risk Factor-Ex-smoker	Ex-smoker (Ex-tobacco user);
Unknown	Relevant Med History Risk Factor-Hyperlipidaemia	Hyperlipidaemia (Hyperlipidaemia);
Unknown	Relevant Med History Risk Factor-Hypertension	Hypertension (Hypertension);
Unknown	Relevant Med History Risk Factor-Peripheral arterial disease	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History Risk Factor-Stroke	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History Aug-2014	Hemodialysis (Haemodialysis);
01-JAN-2015 to Unknown	Past Drug Event Lot number: [UNK]	EPOETIN THETA (EPOETIN THETA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	BULGARIA	21	DEC	1958	57 Years	Female	60.00 kg	16	MAR	2016	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombosisa. tibialisvein [Deep vein thrombosis]
Heart failure [Cardiac failure]
Hypotension [Hypotension]

Case Description: Fatal heart failure, fatal hypotension and thrombosis a. tibialis vein. Epoetin zeta. Hospira-sponsored study report received from an investigator (ref: Bg-014-0025), which refers to a patient. The patient was enrolled in a Hospira sponsored study entitled Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), administered subcutaneously for the treatment of renal anaemia.

(Continued on Additional Information Page)

- ☒ PATIENT DIED Date: 24-APR-2016
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 100 IU/kg, (Continued on Additional Information Page)	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 01-MAY-2015 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
3248197

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-APR-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had no history of smoking. Medical history included hypertensive nephropathy which led to renal failure diagnosed in Dec-2013. The patient was on peritoneal dialysis 4 times per week since 24-Apr-2015. The patient had a longstanding hypertension, which had been treated systemically; and thyrotoxicosis. Her mother died because of kidney failure and endemic nephropathy. In the beginning of 2015, after laboratory examinations, a chronic kidney failure had been determined. In the spring of 2015, on the occasion of CKF the patient conducted peritoneal dialysis. The patient also had relapsing atrial fibrillation (arrhythmia). The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit. Concomitant medications were not reported. On an unknown day in May-2015, the patient started to receive epoetin zeta (Retacrit; lot number unknown, 100 IU/kg/week, 2 dosages/week, subcutaneous) for anemia. From Jan-2016, the patient had impaired blood supply and swelling of the lower extremities. Suddenly 1 month ago, on an unspecified date, the toes of the both became blue colored and appeared ulcerations. A conservative treatment was implemented. The toes of the right foot recovered completely.The second and third toes of the left foot gradually began to turn black. It was decided to wait for their demarcation. At the time of admission the patient had marked lymphoedema of the lower legs. The bandage of the dressing was incised in the ankle and foot. The left foot in its entire distal one third was blackened. The patient had been admitted into the hospital in order to implement amputation in the middle of the foot. Conducted therapy with Sintrom for arrhythmia (RAF). Last dose of Retacrit prior to the event was given on 14-Mar-2016. On 16-Mar-2016, the patient was diagnosed with thrombosis a.tibialis vein. On the same day, the patient was admitted to hospital because of the adverse event. The patient had an impaired general condition; with alterations such as in osteoarthritis. The patient was conscious, with reduced hearing; skin was pale, with an earthy color, contact and adequate. The head and neck were configured properly. There were no jugular venous congestion and no perioral cyanosis. The thoracic cage was bilaterally weakened with vesicular breathing, without wheezing and rales. Arrhythmic heart beats was at 108 beats/min (normal range not reported); ABP (Arterial Blood Pressure) was at 90/60. Abdomen was soft, non-painful during palpation. Has a catheter for intraperitoneal dialysis. Angeological status - bilaterally marked edemas of the both lower legs over the fixation bandages. On the left foot a drygangrene away from the middle of the foot up to the toes was present. There was dilated subcutaneous veins of the lower legs. On the right side - present pulsations of the right popliteal artery of the foot arteries. On the left side, present pulsations of the right popliteal artery and without pulsations distally. On 16-Mar-2016, an ultrasound examination with Doppler of the popliteal arteries bilaterally showed diffusely atheromatous plaques, without stenoses. There were moderately expressed stenoses of the tibial arteries bilaterally. Conclusion was of chronic thrombosis of the tibial arteries bilaterally gangrene of the left [illegible]. On unknown dates, laboratory tests showed the following results: hematocrit at 0.26 L/L, 0.27 L/L, 0.25 L/L, and 0.27 L/L; hemoglobin at 84 g/L, 85 g/L,80 g/L, and 85 g/L; platelet absolute count at 125 g/L, 123 g/L, and 74 g/L; creatinine at 379 umol/L,355 umol/L, and 321 umol/L; discharge from wound showed microbiological evidence of Escherichia coli; coagulation tests showed blood clotting time at 4 minutes, prothrombin time at 49.5%, 35.6%, 35.5%, and 22 sec, 30.5 sec, and 30.6 sec; INR at 2.28, 3.38, and 3.39. On 17-Mar-2016, at a nephrologist consult, blood pressure was at 80/60 (units and normal ranges not reported); liver was at the costal margin, and had an arrhythmic heart rate. A consultative examination by cardiologist was suggested. Iron binding capacity and serum iron have to be examined. On the same day, at a cardiologist consult, arterial blood pressure was 90/60; objective status showed weakened VB (vesicular breathing) without wheezing, and rales; arrhythmic heart rate; and edemas; ECG [Electrocardiogram] - atrial fibrillation. Acid-alkaline balance and serum [illegible] have to be examined. On 18-Mar-2016, the patient was been submitted to amputation of the left foot according to Lisfranc. It was reported that spinal anesthesia (unspecified; dose and route of administration not reported) was used for the operation. The tissues were infected along the boundaries of the demarcation line, which required the total removal of the metatarsal bones. The wound did not been close hermetically, and suture of only 2 stitches was implemented in order to cover the underlying bones. On the 3rd day, the stitches were removed [illegible] formation of bulla [illegible] filled with black hemorrhagic fluid. On the 4th day [illegible] the process spread towards the heel. [illegible] it was decided to carry out an amputation at a higher level. Because of the marked lymph edema of the extremity and the increased risk of spreading of the inflammation because of the severe concomitant diseases of the patient, and the risk of subsequent indispensability general anesthesia to be implemented repeatedly, it was decided to carry out an amputation of the hip level - medium / lower third. On 24- Mar-2016, at a nephrologist consult, the patient was with [illegible] of the lower extremities. Probably because of lymph congestion and hypoalbuminemia. Infusion of Human albumin was suggested. On the same day, at a cardiologist consult,without complains; lungs had intensified vesicular breathing, arterial blood pressure was [illegible] / 80; and an ECG showed relapsing atrial fibrillation. Therapy with Bisogamma (1 tablet; dose and route of administration not reported) was given. On 25-Mar-2016, the cardiologist reduced the dose of Bisogamma to 2.5 mg, daily. On the same date, ABP was 110/ [70]; ECG showed low voltage [illegible]; and echocardiography showed pleural effusion. On the same day, the patient underwent amputation of the left leg through femur using endotracheal anesthesia (unspecified; dose and route of administration not reported). The operation proceeded uneventfully, and without any complications following the implemented amputation of the left leg through the thigh. The wound began to heal primary. Therapeutic scheme was followed by the patient as follows: fraxiparine, Agapurin (1 tablet, 2 times), Omeprazil (1 tablet, 2 times), Cefa (1 g, IV), Flagyl (1 phial, 2 times, during 4 days) until the results of the antibiogram would be ready, after which Ciprinol (200 mg 2 times) would be started; Diroton 10 mg (1/2 tablet, 2 times) which has been discontinued because of hypotension, Sintrom (according to a scheme, daily), (routes of administration not reported); and hemotransfusion of erythrocyte concentrate and plasma. Action taken with the suspect drug was not reported. The patient was discharged from the hospital on 29-Mar-2016 without pain. Primary healing of the operative wound of the amputational stump; satisfactory general condition; ABP at 110/80, afebrile, the patient was undergoing physical therapy, and can stay in a sitting position. Outcome of the adverse event was reported as healed on an unknown date. On an unknown date, the patient experienced heart failure and hypotension. Treatment for the events of heart failure and hypotension were not reported. On 24-Apr-2016, the patient died. Causes of death were heart failure and hypotension. It was unknown if an autopsy was performed. The investigator's opinion of causality between the events of fatal heart failure, fatal hypotension and the suspect drug was not reported while it was unlikely for the event of thrombosis a. tibialis vein. Risk factors included coronary heart disease, atrial fibrillation, and heart failure NYHA stage II. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 27-Apr-2016: Additional information was received from the same

Mfr. Control Number: 3248197

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

reporter. Additional medical history and laboratory/diagnostic tests were provided. Clinical event progression details and treatment for the adverse event were provided. Outcome of the adverse event was updated to recovered (previously was not yet recovered). This information has been incorporated in the narrative and in the corresponding data fields. 10 May 2016: Additional information was received from the same reporter. Fatal heart failure and fatal hypotension were added as adverse events. This information has been incorporated in the narrative and corresponding data fields.

Case Comment: Overall case causality: Related Reporter causality noted, but consider also possible contributory effect of suspect drug for this labeled event, combined with pre-existing and predisposing patient risk factors. Follow-up: No change in previous assessment. Follow-up: No change in assessment for labeled thrombotic event. Consider added events as more likely due to patient comorbidities and CV risk factors.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood creatinine	355 MCMOL/L	
2		Blood creatinine	379 MCMOL/L	
3	17-MAR-2016	Blood creatinine	321 MCMOL/L	
4	17-MAR-2016	Blood pressure measurement	80/60 Unknown	
5	17-MAR-2016	Blood pressure measurement	90/60 Unknown	
6	17-MAR-2016	Blood pressure measurement	110/80 Unknown	
7	25-MAR-2016	Blood pressure measurement	110/70 Unknown	
8	17-MAR-2016	Coagulation time	4 Minutes	
9	25-MAR-2016	Echocardiogram	Pleural effusion	
10	17-MAR-2016	Electrocardiogram	Atrial fibrillation Unknown	
11	24-MAR-2016	Electrocardiogram	Relapsing atrial fibrillation	
12	25-MAR-2016	Electrocardiogram	Low voltage	
13		Haematocrit	0.27 L/L	
14		Haematocrit	0.25 L/L	
15		Haematocrit	0.26 L/L	
16		Haemoglobin	80 g/l	
17		Haemoglobin	84 g/l	
18		Haemoglobin	85 g/l	
19		Heart rate	108 Beats per mintue	
20		International normalised ratio	2.28	
21		International normalised ratio	3.38	

Mfr. Control Number: 3248197

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
22		International normalised ratio	3.39	
23		Microbiology test	Evidence of Escherichia coli	
24		Platelet count	74 g/l	
25		Platelet count	125 g/l	
26		Platelet count	123 g/l	
27		Prothrombin time	30.6 seconds	
28		Prothrombin time	22 seconds	
29		Prothrombin time	30.5 seconds	
30		Prothrombin time	35.5 %	
31		Prothrombin time	49.5 %	
32		Prothrombin time	35.6 %	
33		Ultrasound Doppler	Chronic thrombosis of tibial arteries	
34		Ultrasound Doppler	bilateral gangrene of the left	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	100 IU/kg, 2 dosages/week, Freq: 1 Week; Interval: 1; Subcutaneous	Anemia (Anaemia)	01-MAY-2015 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies and alcohol consumption were not reported. The patient had no history of smoking. Medical history included hypertensive nephropathy which led to renal failure diagnosed in Dec-2013. The patient was on peritoneal dialysis 4 times per week since 24-Apr-2015. The patient had a longstanding hypertension, which had been treated systemically; and thyrotoxicosis. Her mother died because of kidney failure and endemic nephropathy. In the beginning of 2015, after laboratory examinations, a chronic kidney failure had been determined. In the spring of 2015, on the occasion of CKF the patient conducted peritoneal dialysis. The patient was not treated with an erythropoiesis-stimulating agent (ESA) prior to treatment with Retacrit. Risk factors included coronary heart disease, atrial fibrillation, and heart failure NYHA stage II. Race/Ethnicity: Caucasian On 24-Apr-2016, the patient died. Causes of death were heart failure and hypotension. It was unknown if an autopsy was performed.
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown	Relevant Med History	Heart failure NYHA class II (Cardiac failure chronic);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);
Unknown	Relevant Med History Concurrent procedure; 4 times per week	Peritoneal dialysis (Peritoneal dialysis);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Osteoarthritis (Osteoarthritis);
Unknown to Ongoing	Relevant Med History	Thyrotoxicosis (Hyperthyroidism);
Unknown	Relevant Med History Family Medical History	Nephropathy (Nephropathy);
Unknown	Relevant Med History Family Medical History: Mother	Kidney failure (Renal failure);
Unknown	Relevant Med History	Amputation (Amputation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	15	DEC	1941	74 Years	Female	78.00 kg	30	JUN	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
apoplexy [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study for Protocol ID EPOE-09-11, regarding subject ID 471|0041.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 6000 UNK every 2 wekks	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 14-APR-2015 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATORVASTATIN (ATORVASTATIN) ; Unknown
#2) NEPHROTRANS (SODIUM BICARBONATE) ; Unknown
#3) VALSARTAN (VALSARTAN) ; Unknown
#4) TORASEMID (TORASEMIDE) ; Unknown
#5) AMLODIPINE (AMLODIPINE) ; Unknown
#6) APIDRA (INSULIN GLULISINE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Obesity (Obesity)
Unknown to Ongoing	Relevant Med History	Atherosclerosis (Arteriosclerosis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016401625

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-AUG-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 74-year-old female subject was taking subcutaneous epoetin zeta (RETACRIT), 6000 every 2 weeks from 14Apr2015, 4000 every two weeks from an unspecified date, and 6000 every 2 weeks from 04May2016, units unspecified, for renal anemia. The subject's medical history included obesity, atherosclerosis, hyperlipidemia, type 2 diabetes mellitus since 1976 (using insulin), hypertension since 2000, chronic renal insufficiency (GFR 28=stage 3), gout, hyperuricemia, double vessel disease, all ongoing, status post "rip" fracture (Pentecost 2016, as reported). As per the "Somatic history/self-anamnesis" of the medical records, the following was described: the diabetes mellitus type II with insulin, with renal complications: not explained as off-the-rails glomerula diseases at diabetes mellitus. Her concomitant medications included atorvastatin at 40 mg once daily, sodium bicarbonate (NEPHROTRANS) at 840 mg thrice daily, valsartan at 320 mg once daily, torasemide (TORASEMID) at 10 mg once daily and 30 mg 1x/daily for hypertension, amlodipine at 2.5 mg twice daily, insulin glulisine (APIDRA) at 22 IU subcutaneously daily (8 IU in the morning, 4 IU at noon, 10 IU in the evening) and at 60 IU, 3x/daily, and insulin glargine (LANTUS) at 26 IU subcutaneously once daily at night, telmisartan at 20 mg 1x/daily for hypertension, allopurinol at 100 mg 1x/daily for hyperuricaemia, The subject's any other erythropetin-stimulating agent (ESA) included: neorecormon from 09Aug2010 to 14Apr2015 at 4000 IE, haemoglobin value: not known; darbepoetin alfa (ARANESP) from known date to Jan2010 at 20 ug, haemoglobin value: not known. The subject didn't experience any thromboembolic event during treatment with any other ESA. The subject was hospitalized on 01Jul2016 and was diagnosed with posterior media-part infarct left cerebral temporoparietal as well as specific development border zone ischemia on the left side in projection to the anterior and posterior border zones. apoplexy. The event term was reported as apoplexy with onset date of 30Jun2016 and considered medically significant. As per the medical records of the subject's hospitalization from 01Jul2016 to 07Jul2016: Current history: Relocation of the patient from the clinic because of the freshly occurred stroke on the left parietal region with emphasized motoric aphasia, word finding difficulties since yesterday evening 04:30pm: already well unlabeled left sided cerebral infract. Patient was cardiopulmonary stable. Special history: No allergies, no nicotine abuse, no alcohol abuse. Micturition/defecation: normal, no fever/infection. Weight: constant, normal appetite. Psychological/ psychopathologic examination performed on 01Jul2016: normal. Neurological examination performed on 01Jul2016: normal. The subject was receiving complex treatment of stroke including physiotherapy, ergotherapy and logotherapy. The cardiovascular diagnostic (ECG, Holter ECG, transthoracal echocardiography, ECD, Dupplex sonography and chest X-ray) performed no additional relevant etiological result. We complemented acetylsalicylic acid (ASS) 100 mg to the preexisting atorvastatin as secondary prophylaxis. It persist (as reported) hypertension, dyslipidemia and diabetes mellitus type 2 as cardiovascular risks. We reduced the torasemid dose slightly. We request a subsequently cure treatment by still daily routine relevant hemianopsia right. The patient was mobile without any restriction at the discharge. Furthermore, the patient showed a strikingly improved aphasia without relevant restriction of the daily routine communication. However, exists the above mentioned hemianopsia to the right and an agraphia (as reported). Diagnostics: Head MRI, ischemia, performed on 01Jul2016. Total-evaluation: wedge-shaped posterior media - partly infarct on the left side on the temporoparietal, specific development border zone ischemia on the left side in projection to the anterior and posterior border zones. No evidence of a serious vascular encephalopathy. No evidence of a significant atrophy. Flow reduction of the left ACI in question compared to right as well as mild siphon stenosis on the left side. Doppler, Duplex sonography of extracranial vessels on 04July2016. Assessment: no sign for extracranial stenosis. MRI extra-/intracranial vessels, 'MRA' on 07July2016. Especially higher-grade stenosis of the ACI II close to skull base, otherwise ACI progress is inconspicuous (authorized finding outstanding). Chest X-ray, 1 tier, on 04July 2016: Overall assessment: no evidence of infiltration and pulmonic venous stasis. ECG by the bed on 04July 2016: Left type, SR with normal frequency, Heart rate 72/min, normal QTc-time. Long-term ECG on 04July2016: Assessment: plentiful artifacts due to dissolved electrodes-probably permanent SR. Transthoracic echocardiography on 04July 2016: No sign on cardiac embolism. Partial infarct left temporoparietal and described cross zones ischemia left in projection of the frontal and rear border zone left by evidently preceding intracranial skull base near stenosis from the internal carotid artery left. The subject was discharged on 07Jul2016. The action taken with epoetin zeta in response to the event was not reported. Outcome of event was reported as: persistent/significant disability (persistent hemianopsia, hemiparesis recovered).

Per the investigator: the causal relationship to epoetin zeta was assessed as unlikely.

Follow-up (24Aug2016): Updates reaction details, subject data, study drug data, medical history, concomitant medications, tests and treatment, adds medical record information.

Follow-up (02Sep2016): Correction of previously reported data: medical history: status post rib fracture Pentecost 2016 was reported.

Follow-up (03Aug2018): New information from the investigator includes: new lab data and past drug, torasemide updated indication and new dosage, insulin glulisine new dosage, new concomitant drugs telmisartan and allopurinol, updated event outcome and investigator causality assessment.

Case Comment: The information provided so far does not support a causal association between the study medication and the reported event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-JUL-2016	Activated partial thromboplastin time	30 seconds	36 26
2	01-JUL-2016	Blood cholesterol	7.13 mmol/l	6.2

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
3	01-JUL-2016	Blood creatinine	143 umol	88
4	02-JUL-2016	Blood creatinine	167 umol	88
5	01-JUL-2016	Blood urea	15.31 mmol	8.3 1.7
6	02-JUL-2016	Blood urea	17.73 mmol	8.3 1.7
7	01-JUL-2016	C-reactive protein	less than 5 mg/l	10
8	04-JUL-2016	Echocardiogram	No sign on cardiac embolism	
9	04-JUL-2016	Electrocardiogram	plentiful artifacts due to dissolved electrodes-pr	
10	04-JUL-2016	Electrocardiogram	Left type, SR with normal frequency	
11	04-JUL-2016	Electrocardiogram QT interval	normal	
12	01-JUL-2016	Glomerular filtration rate	33 ml	140 80
13	02-JUL-2016	Glomerular filtration rate	28 ml	140 80
14	01-JUL-2016	Haematocrit	0.33	0.47 0.35
15	02-JUL-2016	Haematocrit	0.30	0.47 0.35
16		Haemoglobin	mmol/l	9.8 7.3
17		Haemoglobin	mmol/l	9.8 7.3
18	03-FEB-2016	Haemoglobin	6.8 mmol/l	9.8 7.3
19	04-MAY-2016	Haemoglobin	6 mmol/l	9.8 7.3
20	01-JUL-2016	Haemoglobin	7.20 mmol/l	9.8 7.3
21	02-JUL-2016	Haemoglobin	6.4 mmol/l	9.8 7.3
22	04-JUL-2016	Heart rate	72	
23	01-JUL-2016	High density lipoprotein	1.56 mmol	 1.68
24	01-JUL-2016	Investigation	normal	
25	01-JUL-2016	Low density lipoprotein	4.73 mmol/l	4
26	01-JUL-2016	Lymphocyte count	22.3 %	51 20
27	01-JUL-2016	Magnetic resonance imaging	ischemia	
28	07-JUL-2016	Magnetic resonance imaging	Especially higher-grade stenosis of the ACI II clo	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
29	01-JUL-2016	Neurological examination	normal	
30	01-JUL-2016	Platelet count	224 x10 9/l	355 128
31	02-JUL-2016	Platelet count	213 x10 9/l	355 128
32	01-JUL-2016	Prothrombin time	1	1.25 0.95
33	01-JUL-2016	Prothrombin time	100 %	 70
34	01-JUL-2016	Red blood cell count	3.74 x10 12/l	5.2 3.8
35	02-JUL-2016	Red blood cell count	3.36 x10 12/l	5.2 3.8
36	04-JUL-2016	Ultrasound scan	no sign for extracranial stenosis	
37	01-JUL-2016	White blood cell count	7.7 x10 9/l	11.8 3.6
38	02-JUL-2016	White blood cell count	6 x10 9/l	11.8 3.6
39	04-JUL-2016	X-ray	no evidence of infiltration and pulmonic venous st	

13. Relevant Tests

Chest X-ray, 1 tier (04Jul2016): Overall assessment: no evidence of infiltration and pulmonic venous stasis
ECG by the bed (04Jul2016): Left type, SR with normal frequency, Heart rate 72/min, normal QTc-time
Long-term ECG (04Jul2016):plentiful artifacts due to dissolved electrodes-probably permanent SR
MRI (01Jul2016): ischemia. Total-evaluation: wedge-shaped posterior media - partly infarct on the left side on the temporoparietal, specific development border zone ischemia on the left side in projection to the anterior and posterior border zones. No evidence of a serious vascular encephalopathy. No evidence of a significant atrophy. Flow reduction of the left ACI in question compared to right as well as mild siphon stenosis on the left side.
MRI extra-/intracranial vessels (07Jul2016): Especially higher-grade stenosis of the ACI II close to skull base, otherwise ACI progress is inconspicuous (authorized finding outstanding).
Transthoracic echocardiography (04Jul2016): No sign on cardiac embolism. Partial infarct left temporoparietal and described cross zones ischemia left in projection of the frontal and rear border zone left by evidently preceding intracranial skull base near stenosis from the internal carotid artery left.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	4000 UNK, every 2 weeks; Subcutaneous	renal anaemia (Nephrogenic anaemia)	Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	6000 UNK, every 2 weeks; Subcutaneous	renal anaemia (Nephrogenic anaemia)	04-MAY-2016 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LANTUS (INSULIN GLARGINE) ; Unknown

#8) TELMISARTAN (TELMISARTAN) ; Unknown

#9) ALLOPURINOL (ALLOPURINOL) ; Unknown

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
1976 to Ongoing	Relevant Med History Using insulin	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
2000 to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History GFR 28=stage 3	Chronic renal insufficiency (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Gout (Gout);
Unknown to Ongoing	Relevant Med History	Hyperuricemia (Hyperuricaemia);
Unknown to Ongoing	Relevant Med History	Double vessel disease (Coronary artery disease);
2016 to Unknown	Relevant Med History Pentecost 2016	Rib fracture (Rib fracture);
09-AUG-2010 to 14-APR-2015	Past Drug Event at 4000 IE, haemoglobin value: not known	neorecormon (NEORECORMON);
Unknown to JAN-2010	Past Drug Event at 20 ug, haemoglobin value: not known	Aranesp (ARANESP);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		OCT	1938	77 Years	Male	67.50 kg	25	JUN	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Middle cerebral artery infarction [Cerebral infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer-sponsored, non-interventional study, protocol EPOE-09-11, regarding subject 093 0082.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 18000 IU, weekly (mean dose)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 08-JAN-2014 / 29-JUN-2016

19. THERAPY DURATION
#1) 904 days

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hemodialysis (Haemodialysis)
Unknown to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016428437

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-SEP-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 77-year-old Caucasian male subject started epoetin zeta (RETACRIT), administered subcutaneously three times a week (mean weekly dose 18000 IU) on 08Jan2014 for the study indication of renal anemia. His hemoglobin on 04Apr2016 was 11.3 g/dl (range 12.5 - 17) and 12.1 g/dl on 23May2016. The subject's medical history included hemodialysis, ischemic heart disease, peripheral arterial disease since Jul2014, diabetes mellitus and hypertension. No concomitant medications were reported. On 25Jun2016, the subject was hospitalized on an emergency basis to the neurological ward approximately 40 minutes after he felt dizziness and fainted. When he regained consciousness, he could not move his left arm or left leg and his speaking abilities had changed, becoming more incomprehensible. Initially Skull-CT and a CT-A were performed with no signs of fresh ischemia, no signs of ACM-occlusion, bleeding or masses. The subject was relocated to the stroke unit for further monitoring. Clinical neurological findings: Subject well oriented, cooperative to all qualities. Cranial nerves: Pupils round, isocor, light responding, visual field normal, slight mouth dysmetry on the left side, no aphasia, moderate dysarthria, motor and reflex: Movement ability: right (upper and lower extremities) 5/5, left: upper extremities: 0-1/5, lower extremities: 0-1/5. Babinski both sided negative. Sensitivity: normal. Extrapyramidal nervous system: no rigor, no tremor, no hyper- or hypokinesis. Tests included: Skull computed tomography (CT) with 3d- angiography of the intracranial vessels on 29May2016: Even in the non-contrast medium CT, small, round calcified lesions (about 3 mm, Ima 55/6) with contact to the vascular system can be see which is consistent with aneurysm in a branch of the arteria basilaris (Anterior inferior cerebellar artery (AICA). Carotid extracranial duplex sonography on 30Jun2016: extended arteriosclerotic vasculopathy; no indication of hemodynamic relevant stenosis or closure. Chest X-ray (supine) on 02Jul2016: Cardiomegaly with low to moderate chronic pulmonary congestion or hyperhydration, bilateral angle effusions, no inflammatory pulmonary infiltrates. Chest X-ray on 12Jul2016: New enclosed subcutaneous implantable cardioverter/ defibrillator left in comparison to the pre-investigation. Sheldon-catheter is projected on the vena cava superior. Increased signs of congestion established on the pre-investigation. Pleural effusion right. No proof infiltrates. Unchanged imagining from the cardiac silhouette by status after coronary artery bypass grafting. Calcification of the aortic wall. The event was reported as middle cerebral artery infarction with an onset date of 29Jun2016. The event was also considered serious due to disability. Course: The subject was admitted for monitoring to our stroke unit due to suspected fresh infarct of the right side of the brain with prominent senso-motoric hemiparesis on the left side. The initial skull-CT and CT-A (29Jun2016) showed no signs of a fresh ischemia or a marked ACM-occlusion, so that no intervention was needed. In the follow-up skull-CT (30Jun2016) hypodensities were found ventrally to the anterior horn of the ventriculus cerebri as well as in the area of putamen and the crus posterior of the capsula interna on the right side, which match the clinical picture. No high grade cardiac arrhythmias were found either on the ECG nor on the ECG monitoring in the stroke unit. The blood pressure monitoring also showed no abnormalities. The HbA1c value was below 5.9%. The subject was monitored in our stroke unit for 72 hours; the neurological symptoms were slightly improved. No action was taken with the study drug in response to the event. It was reported, on 04May2016, the Sheldon catheter system, was inserted. Venous puncture was difficult, with an incorrect arterial puncture of the left a. carotis. Eventual successful puncture of the v. subclavian sinistra with a 20 cm Shaldon catheter. On 06Jul2016, the subject developed a shivering attack (dialysis running through a Sheldon catheter system which had been inserted 04Jul2016). On 12Jul2016, the subject was discharged to a geriatric rehabilitation facility. Discharge diagnoses: Fresh ischemia ventral to the anterior horn of the ventriculus cerebri as well as in the area of the putamen and the crus posterior of the capsula interna on the right side with Hemiparesis most prominent in the left arm; NIHSS National Institute of Health Stroke Scale upon admission with 6 points in the presence of hemiparesis prominent on the arm with dysarthria; NIHSS at discharge with 5 points with paresis on the left arm with hemiparesis prominent on the arm as well as dysarthria; Removal of Demers catheter via vascular surgery on 08Jul2016; Sheldon catheter through the anesthesia on the 04Jul2016 (Recommendation: Chlorhexidin bandage); Renal insufficiency requiring dialysis (Dialysis Monday-Wednesday-Friday); Diabetes mellitus. His discharge medications included: tilidin, simvastatin (SIMVASTIN), allopurinol, acetylsalicylic acid (ASS), tamsulosin, calcitriol (OSTEOTRIOL), eplerenone, carvediol, clopidogrel (PLAVIX), furosemide (FURORESE), candesartan, pantoprazole (PANTOZOL), formoterol, metamizole (NOVALGIN), human insulin (ACTRAPID), protaphane, heparin, terracid and epoetin zeta. Course at rehabilitation facility: High inflammation values were shown on admission. A staphylococcus epidermidis appeared in the blood count and on the tip of the removed Sheldon-catheter. Treatment included Vancomycin, with subsequent reduction in the inflammatory values. A transesophageal echocardiography (TEE) was performed, which showed no relevant valve vegetation, but a floating structure in the V. cava superior. In the follow-up one week later, the structure was still measurable, so assumption made it was a parietal thrombus after Demers-catheter-facility. Attempts were made to release the dialysis under diuretic therapy with selective nephron block initially. In the process, treatment with hygroton was stopped and torasemide dose was reduced to 40 mg daily. Initially, the diuretic therapy led to an increase in renal retention values with creatinine of 2.6 mg/dl and urea 200 mg/dl. After reduction of the diuretic therapy the values declined. Enoxaparin treatment was started. After inflammation values dropped, treatment with vancomycin was stopped. The inflammation values once again increased. The focus search showed a 3 MRGN E. coli in the urine which was treated with cotrimoxazol and then with meropenem after the inflammation values increased even more. Additional tests included: Urine culture on 16Jul2016: E.coli more than 10^5 CFU/ml, 3 multi-resistant gram-negative pathogens E. coli; TEE on 15Jul2016: No hints of mobile structures/vegetation on all four native valves, no enclosed foreign material (has subcutaneous implantable cardioverter/defibrillator system) furthermore floating structure in vena cava superior are measurable, which are smooth and reach shortly the right atrium. On 25Jul2016, creatinine 2.5 mg/dl (range 0.7 - 1.2), lactate dehydrogenase (LDH) 174 IU/l (range 135 - 225), urea 194 mg/dl (range 18 - 55), gamma-glutamyltransferase (Gamma GT) 907 IU (range 8 - 61), hematocrit 32.3% (range 37 - 49), hemoglobin 10.8 g/dl, platelet count (PLT) 347x10 3/mm3 (range 160 - 370), red blood cell count (RBC) 3.72x10 6/mm3 (range 3.99 - 5) and white blood cell count (WBC) 5.6x10 3/mm3 (range 3.6 - 10.5). On 26Jul2016, urea 190 mg/dl and hemoglobin 10.5 g/dl. On 27Jul2016, glucose 72 mg/dl (range 82 - 115), LDH 176 IU/l and Gamma GT 929 IU. On 28Jul2016, creatinine 2.1 mg/dl, glucose 125 mg/dl, LDH 180 IU/l, urea 191 mg/dl and Gamma GT 827 IU. On 29Jul2016, creatinine 1.8 gm/dl, LDH 188 IU/l, urea 187 mg/dl, hematocrit 30.6%, hemoglobin 10.1 g/dl, mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC) and mean cell volume (MCV), all 3 reported as normal, PLT 256x10 3/mm3, RBC 3.54x10 6/mm3 and WBC 5.5x10 3/mm3. Clinic-pathological result: Multiple hematomas, raccoon eyes. No irritated cicatrices after implantable cardioverter defibrillator and bypass operation, gynecomastia. Arm focused paresis left, Grade of strength 2-3.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Muscle reflexes left increased, Babinski left positive. By absorption not mobilizable. Diagnoses: 1. Ischemic media partial infarct right, hemiparesis prominent on left arm, dysarthria, 2. Ischemic cardiomyopathy at coronary 3-vessel-disease, Primary prophylactic ICD-implantation on 30May2016, Coronary angiography 06.April2016: bare-metal stent-implantation in the RCA, intact bypass IMA ad RIVA, EV ad CX, 75% RCX stenosis, 75% main stem stenosis, 4. Chronic renal insufficiency a.e. cardio-renal syndrome, Status post Demers-catheter-infection and Sheldon- facility on 04Jul2016, Currently: Sheldon-catheter-infection through staphylococcus epidermidis, 5. Urinary infection through 3MRGN E-coli, 6.Flottfloating structure in the V.cava superior, 7. An e. parietal thrombus after Demers-catheter-facility, 8. pAVK-Status post stent of the A.iliaca right 07/2009, 9. Status post ventral decompression and fusion HWK 5-7 2005 at intervertebral disc protrusion, 10. Anamnetic known osteoporosis-Status post LWK 3 fractures, 11. Asbestosis, 12. Silicosis. Functional status at admission: Activities of daily living (ADL): help with all, Barthel-index 10 points. Functional status at discharge: Functional improvement of the hemiparesis left side. Improvement through logopedic training. The subject was discharged from the geriatric rehabilitation facility on 03Aug2016. The subject had not recovered from the event. The investigator reported there was no reasonable possibility that the event, middle cerebral artery infarction, was related to the study drug, any concomitant medication or to a clinical trial procedures was not provided.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, middle cerebral artery infarction, was related to the study drug, or associated with a clinical trial procedure. Epoetin zeta started around 1.5 years before the onset of the event. Underlying ischemic heart disease, peripheral arterial disease, diabetes mellitus and hypertension provided the most likely explanations for the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	25-JUL-2016	Blood creatinine	2.5 mg/dl	1.2 0.7
2	28-JUL-2016	Blood creatinine	2.1 mg/dl	1.2 0.7
3	29-JUL-2016	Blood creatinine	1.8 mg/dl	1.2 0.7
4	13-JUL-2016	Blood culture	Staphylococcus epidermis	
5	27-JUL-2016	Blood glucose	72 mg/dl	115 82
6	28-JUL-2016	Blood glucose	125 mg/dl	115 82
7	25-JUL-2016	Blood lactate dehydrogenase	174 IU/l	225 135
8	27-JUL-2016	Blood lactate dehydrogenase	176 IU/l	225 135
9	28-JUL-2016	Blood lactate dehydrogenase	180 IU/l	225 135
10	29-JUL-2016	Blood lactate dehydrogenase	188 IU/l	225 135
11	25-JUL-2016	Blood urea	194 mg/dl	55 18
12	26-JUL-2016	Blood urea	190 mg/dl	55 18
13	28-JUL-2016	Blood urea	191 mg/dl	55 18
14	29-JUL-2016	Blood urea	187 mg/dl	55 18
15	14-JUL-2016	Catheter culture	Evidence staphylococcus epidermis	
16	02-JUL-2016	Chest X-ray	Cardiomegaly	
17	12-JUL-2016	Chest X-ray	Pleural effusion right	
18	29-MAY-2016	Computerised tomogram head	Round calcified lesions	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
19	30-JUN-2016	Computerised tomogram head	Hypodensities	
20	16-JUL-2016	Culture urine	E. coli	
21	15-JUL-2016	Echocardiogram	no mobile structures/vegetation on valves	
22	25-JUL-2016	Gamma-glutamyltransferase	907 IU	61 8
23	27-JUL-2016	Gamma-glutamyltransferase	929 IU	61 8
24	28-JUL-2016	Gamma-glutamyltransferase	827 IU	61 8
25	25-JUL-2016	Haematocrit	32.3 %	49 37.0
26	29-JUL-2016	Haematocrit	30.6 %	49 37.0
27	04-APR-2016	Haemoglobin	11.3 g/dl	17 12.5
28	23-MAY-2016	Haemoglobin	12.1 g/dl	17 12.5
29	25-JUL-2016	Haemoglobin	10.8 g/dl	17 12.5
30	26-JUL-2016	Haemoglobin	10.5 g/dl	17 12.5
31	29-JUL-2016	Haemoglobin	10.1 g/dl	17 12.5
32	29-JUL-2016	Mean cell haemoglobin	normal	
33	29-JUL-2016	Mean cell haemoglobin concentration	normal	
34	29-JUL-2016	Mean cell volume	normal	
35	25-JUL-2016	Platelet count	347 x10 3/mm3	370 160
36	29-JUL-2016	Platelet count	256 x10 3/mm3	370 160
37	25-JUL-2016	Red blood cell count	3.72 x10 6/mm3	5 3.99
38	29-JUL-2016	Red blood cell count	3.54 x10 6/mm3	5 3.99
39	30-JUN-2016	Ultrasound Doppler	No hemodynamic relevant stenosis	
40	25-JUL-2016	White blood cell count	5.6 x10 3/mm3	10.5 3.6
41	29-JUL-2016	White blood cell count	5.5 x10 3/mm3	10.5 3.6

13. Relevant Tests

Skull computed tomography (CT) w/3D- angiography intracranial vessels (29May2016): Even in the non-contrast medium CT, small, round calcified lesions (about 3 mm, Ima 55/6) with contact to the vascular system can be seen, consistent with aneurysm in a branch

ADDITIONAL INFORMATION

13. Relevant Tests

of the arteria basilaris (Anterior inferior cerebellar artery (AICA).
Skull CT (30Jun2016): hypodensities were found ventrally to the anterior horn of the ventriculus cerebri as well as in the area of putamen and the crus posterior of the capsula interna on the right side, which match the clinical picture. Differential diagnosis possible subacute ischemia, differential diagnosis microangiopathy.
Carotid extracranial duplex sonography (30Jun2016): extended arteriosclerotic vasculopathy; No indication of hemodynamic relevant stenosis or closure.
Culture Sheldon catheter (14Jul2016): Evidence of staphylococcus epidermis < 15 CFU
Blood culture (13Jul2016): Staphylococcus epidermis anaerobe an aerobe
Urine culture (16Jul2016): E.coli more than 10^5 CFU/ml, 3 multiresistant gram-negative pathogens E.coli
TEE (15Jul2016): No hints of mobile structures/vegetation on all four native valves, no enclosed foreign material (has subcutaneous implantable cardioverter defibrillator - system) furthermore floating structure in vena cava superior are measurable, which are smooth and reach shortly the right atrium.
Chest X-ray (supine) (02Jul2016): Cardiomegaly with low to moderate chronic pulmonary congestion or hyperhydration, bilateral angle effusions, no inflammatory pulmonary infiltrates.
Chest X-ray (12Jul2016): New enclosed subcutaneous implantable cardioverter defibrillator left in comparison to the Preinvestigation. Sheldon-catheter is projected on the vena cava superior. Increased signs of congestion established on the Preinvestigation. Pleural effusion right. No proof infiltrates. Unchanged imagining from the cardiac silhouette by status after coronary artery bypass grafting. Calcification of the aortic wall.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
JUL-2014 to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	BULGARIA	30	MAY	1943	73 Years	Male	80.00 kg	23	SEP	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Ischemic brain stroke [Ischaemic stroke]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non-interventional Study for Protocol EPOE-09-11, regarding subject BG-004-0038.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 2000 IU, UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 06-FEB-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) TRIFAS (ETHINYLESTRADIOL, NORGESTIMATE) ; Ongoing
#2) CARVEDIL (CARVEDILOL) ; Ongoing
#3) MILURIT (ALLOPURINOL) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History ischemic heart attack	Ischemic heart disease (Myocardial ischaemia)
Unknown	Relevant Med History	Heart attack (Myocardial infarction)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016536977

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-NOV-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 73-year-old Caucasian male subject started epoetin zeta (RETACRIT) 2000 IU subcutaneously on 06Feb2014 for renal anemia. The most recent dose frequency before the event was 2000 IU every 5th day. The subject's medical history included ischemic heart disease, ischemic heart attack, arterial hypertension, chronic kidney disease, and chronic pyelonephritis. Concomitant medications included torasemide (TRIFAS) 10 mg once daily, carvedilol (CARVEDIL) 3.125 mg once daily, both for hypertension, and allopurinol (MILURIT) 100 mg once daily taken for gout, all ongoing. The subject received 2 independent values of mean doses applied within the period of 3 months prior to the event: Mean dose 1 on 25Apr2016 (with hemoglobin (HGB) 12.6 g/dl and mean dose 2 on 23Sep2016 (with HGB 13.8 g/dl) which had no changes to the dose regimen. He was not exposed to any other erythropoietin-stimulating agent and did not experience any thromboembolic event during treatment with any other ESA. There were no other risk factors reported. On 23Sep2016, the subject experienced ischemic brain stroke and was admitted to hospital. The event was considered life threatening and the subject was hospitalized. Test data included ESR 35 mm, RBC 4.48 T/l (x10 12/l), MCV-95 fl, HCT 0.43 l/l, PLT 200 g/l, WBC 5.9 g/l, HGB (M) 138 g/l, MCH 30 pg; MCHC 322 g/l, PT 89%, INR 1.13, ASAT 25, ALAT 18, potassium 5.53 mmol/l, sodium 136 mmol/l, chloride 108 mmol/l, glucose 9.9 mmol/l, triglycerides 1.2 mmol/l, cholesterol 5.8 mmol/l, creatinine 323 mkmol/l, urea 16.0 mmol/l, bilirubin negative, urobilinogen not increased, ketones mmol/l, glucose qualitative negative, urine showed positive for protein, urine RBC: 300 c/mkl, pH 7, urine positive for nitrite, urine WBC: 500 c/mkl, urine sediment showed bacterium, leukocytes, erythrocytes; glucose 6.0 mmol/l, RBC 4.40T/l (x10 12/l), MCV 96 fk, HCT 0.42 l/l, PLT 179 g/l, WBC 5.4 g/l, HGB (M) 132 g/l, MCH 30 pg, MCHC 314 g/l, glucose 5.8 mmol/l, EEG showed not well organized alpha rhythm and diffuse changes, CT multi-infarct encephalopathy, cortical atrophy, and X-ray-showed chylous pulmonary congestion. He was diagnosed as having ischemic insult, left-sided hemiparesis and multi-infarct encephalopathy. The action taken with the study drug was unknown. Treatment included sodium chloride 0.9%, citiciline (SOMAZINA) and metoclopramide hydrochloride (DEGAN). The subject was discharged on 27Sep2016 and considered recovered with sequel on the same day (persistent significant disability). The investigator reported the event of ischemic brain stroke was possibly related to epoetin zeta.

Follow-up (21Nov2016): Confirms medical history ischemic heart attack, seriousness criteria of life-threatening and subject was hospitalized.

Case Comment: On the basis of the available information, the Company considers that the reported event, ischemic brain stroke, is possibly related to the treatment with epoetin zeta. Epoetin zeta can theoretically increase the risk of thromboembolic events based on mechanism of action.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Alanine aminotransferase	18	
2		Aspartate aminotransferase	25	
3		Blood bilirubin	Negative	
4		Blood chloride	108 mmol/l	
5		Blood cholesterol	5.8 mmol/l	
6		Blood creatinine	323	
7		Blood glucose	5.8 mmol/l	
8		Blood glucose	6.0 mmol/l	
9		Blood glucose	9.9 mmol/l	
10		Blood ketone body	1 mmol/l	
11		Blood potassium	5.53 mmol	
12		Blood sodium	136 mmol	
13		Blood triglycerides	1.2 mmol/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
14		Blood urea	16.0 mmol	
15		Computerised tomogram	multi-infarct encephalopathy	
16		Electroencephalogram	not well organized alpha rhythm and diffuse change	
17		Glucose urine	Negative	
18		Haematocrit	0.43	
19		Haematocrit	0.42	
20		Haemoglobin	132 g/l	
21		Haemoglobin	138 g/l	
22	25-APR-2016	Haemoglobin	12.6 g/dl	
23	23-SEP-2016	Haemoglobin	13.8 g/dl	
24		International normalised ratio	1.13	
25		Mean cell haemoglobin	30 pg	
26		Mean cell haemoglobin	30 pg	
27		Mean cell haemoglobin concentration	322 g/l	
28		Mean cell haemoglobin concentration	314 g/l	
29		Mean cell volume	96	
30		Mean cell volume	95	
31		Nitrite urine	Positive	
32		Platelet count	200 g/l	
33		Platelet count	179 g/l	
34		Prothrombin time prolonged	89 %	
35		Red blood cell count	4.48 x10 12/l	
36		Red blood cell count	4.40 x10 12/l	
37		Red blood cell sedimentation rate	35	
38		Red blood cells urine	300	

Mfr. Control Number: 2016536977

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
39		Urinary sediment present	bacterium and erythrocytes	
40		Urine protein, quantitative	Positive	
41		Urobilinogen urine	not increase	
42		White blood cell count	5.9 g/l	
43		White blood cell count	5.4 g/l	
44		White blood cells urine	500	
45		X-ray	showed chylous pulmonary congestion	
46		pH body fluid	7	

13. Relevant Tests

Urine sediment (Date unknown): bacterium, leucocytes and erythrocytes
CT (Date unknown): multi-infarct encephalopathy and cortical atrophy
X-ray (Date unknown): showed chylous pulmonary congestion
EEG (Date unknown): not well organized alpha rhythm and diffuse changes
ESR (Date unknown): 35 mm
HCT (Date unknown): 0.43 l/l
RBC Urine (Date unknown): 300 c/mkl
WBD Urine (Date unknown): 500 c/mkl,
MCV (Date unknown): 95 fk
MCV (Date unknown): 96 fk

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension arterial (Hypertension);
Unknown	Relevant Med History	Chronic kidney disease (Chronic kidney disease);
Unknown	Relevant Med History	Chronic pyelonephritis (Pyelonephritis chronic);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1939	77 Years	Male	82.00 kg	25	JUN	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

death [Death]
NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study for protocol EPOE-09-11. This 77-year-old male subject started epoetin zeta (RETACRIT)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 07-OCT-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 IU, once weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) anemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 19-JUN-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) RAMIPRIL (RAMIPRIL) ; DEC-2014 / Ongoing
#2) BISOPROLOL (BISOPROLOL) ; 13-JUN-2015 / Ongoing
#3) TORASEMID (TORASEMIDE) ; DEC-2014 / Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
OCT-2000 to Unknown	Relevant Med History	Coronary bypass (Coronary artery bypass)
Unknown	Relevant Med History	Surgery (Surgery)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016542530

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-APR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

subcutaneous at 2000 IU once weekly from 19Jun2015 for anemia. There was no pre-dialysis. Last administration prior to event onset was on 03Oct2016. Drug dose of Epoetin-Zeta had not been changed in the 3 months prior to event onset date. The subject's medical history included: coronary bypass operation in Oct2000 and surgery. The patient did not receive any other erythropoietin-stimulating substances. The patient was not obese, did not smoke and had no coagulation disorders. Recent surgeries included trans-apical aortic valve replacement in Oct2013. Medical history further included: ongoing ischemic heart disease since 2000 with status post ACVB (aorto-coronary venous bypass), ongoing peripheral arterial occlusive disease with unknown start date and status post PTA (percutaneous transluminal angiography) of both leg veins, hypertension since 1994 and ongoing. Concomitant medications included ongoing ramipril for hypertension Dec2014, bisoprolol for hypertension orally from 13Jun2015, torasemid for hypertension orally from Dec2014. During MV last Friday, unreported death, reason unknown, was detected for subject Ge-454-0042. The subject died on 07Oct2016. The subject experienced Non STEMI from 25Jun2016 to 26Jun2016 (PCTA with stenting on 25Jun2016), considered life threatening with outcome of recovered. At the start of Epoetin-Zeta on 19Jun2015 hemoglobin was 10.8 g/dl. On 11Aug2016 hemoglobin was 12.5 g/dl and on 16Mar2016 it had been 12.6 g/dl. Blood pressure was 150/80 and neurological examination was normal on unspecified date. The action taken in response to the event with epoetin zeta was unknown. The investigator assessed the event Non STEMI as unrelated to study drug, concomitant medication. The reporter's causality between the event of death and the suspect drug, any concomitant drug or clinical trial procedure, were not reported. Cause of death: cardiac arrest (not determined by autopsy).

The reporter's assessment of the causal relationship of the event death with suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

Follow-up attempts completed. No further Information expected.

Follow-up (02Mar2018): New information received from the investigator included: added new event (NSTEMI), patient information, medical history, concomitant drug, drug dosage regimen, cause of death, causality.

Follow-up (10Apr2018): This is a Non-Interventional Study follow-up report downloaded from the European Medicines Agency (EMA) EudraVigilance-WEB [additional case identifier: DE-EMA-DD-20180312-ngevhprod-160050 and regulatory authority number DE-BFARM-16401697.

New information received included updated death information (autopsy was not done).

No follow-up attempts needed, follow-up automatically provided by EMA.

Follow-up (23Apr2018): This is a follow-up report to notify that case 2016542530 and case 2018081974 are duplicate. All subsequent follow-up information will be reported under 2016542530.

Follow-up (25May2018): New information received from the investigator includes: start date, stop date, indication of suspect drug, lab data, medical history.

Follow-up (11Jul2018): New information received from report downloaded from the European Medicines Agency (EMA) EudraVigilance-WEB with new Sender's case number: DE-EMA-DD-20180620-ngevhprod-155429.

No follow-up attempts needed, follow-up automatically provided by EMA.

Follow-up (26Mar2019): New information received from the investigator included: patient age at event onset (both events) was: 77 years.

Amendment: This follow-up report is being submitted to amend previously reported information: patient ID amended and narrative consolidated.

Case Comment: The information available in this report is limited, and does not allow a medically meaningful assessment of the case. The event "death" with unknown cause is assessed as related to the suspect drug per company guidance. The Company considers there is not a reasonable possibility that the reported event NSTEMI is related to EPOETIN ZETA and is most likely due to patient's preexistent comorbidities such as hypertension and coronary bypass operation. The impact of this report on the benefit/risk profile of the Pfizer product is evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators, as appropriate. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood pressure measurement	140/80 mmHg	

Mfr. Control Number: 2016542530

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
2	19-JUN-2015	Haemoglobin	10.8 g/dl	
3	16-MAR-2016	Haemoglobin	12.6 g/dl	
4	11-AUG-2016	Haemoglobin	12.5 g/dl	
5		Neurological examination	normal	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
OCT-2013 to OCT-2013	Relevant Med History	Aortic valve replacement (Aortic valve replacement);
2000 to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia); status post ACVB (aorto-coronary venous bypass)
Unknown to Ongoing	Relevant Med History	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease); status post PTA (percutaneous transluminal angiography) of both leg veins
1994 to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	FINLAND	20	DEC	1957	58 Years	Male	80.00 kg	08	NOV	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Pfizer non-interventional study, EPOE-09-11, regarding subject FIN001|0005.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU every 5th day

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 11-FEB-2015 / 10-OCT-2016

19. THERAPY DURATION
#1) 608 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPIN /00972401/ (AMLODIPINE) ; Unknown
#2) BISOPROLOL (BISOPROLOL) ; Unknown
#3) FUROSEMIDE (FUROSEMIDE) ; 09-MAR-2012 / Unknown
#4) TELMISARTAN (TELMISARTAN) ; Unknown
#5) MOXONIDINE (MOXONIDINE) ; 19-MAR-2012 / Unknown
#6) SODIUM BICARBONATE (SODIUM BICARBONATE) ; 22-SEP-2016 / Unknown **(Continued on Additional Information Page)**

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1995 to Ongoing	Relevant Med History	Type 1 diabetes mellitus (Type 1 diabetes mellitus)
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016557897

25b. NAME AND ADDRESS OF REPORTER
Sari Aaltonen

FINLAND

24c. DATE RECEIVED BY MANUFACTURER
01-APR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 58-year-old male subject received epoetin zeta (RETACRIT) intravenously from 11Feb2015 to 08Nov2016 for the study indication of renal anemia. Mean dose 1 on 07Aug2016 was 10 000 IU every 5th day (hemoglobin 81 g/l), mean dose 2 on 11Oct2016 was 10 000 IU every 3rd day (hemoglobin 79 g/l). The dose was changed on 11Oct2016, with new dose 10 00 IU every 3rd day. Hemoglobin prior to dose change was 79 g/l and after the dose change was 80 g/l. Medical history included type 1 diabetes mellitus since 1995, hypertension, hypothyreosis, and hyperlipidemia, all ongoing. Concomitant medications included amlodipine 10 mg once daily, bisoprolol 10 mg twice daily, furosemide 375 mg twice daily from 09Mar2012, telmisartan 80 mg once daily, moxonidine 0.4 mg twice daily from 19Mar2012, prazosin 3 mg three times daily from 16Nov2016, all six for hypertension, sodium bicarbonate 1 g once daily from 22Sep2016 for acidosis, benzylpenicillin (PENICILLIN) 3 million IU three times daily from 26Sep2016 to 18Oct2016 for wound infection, dalteparine 2500 IU in dialysis from 12Sep2016 for dialysis, insulin lispro 24 IU three times daily and insulin detemir 30 IU twice daily from 10Feb2016, both for diabetes, ceftriaxone 2 g once daily from 11Sep2016 to 26Sep2016 and unspecified dose from 10Nov2016 to 16Nov2016 for septicemia, acetylsalicylic acid (ASA) 100 mg once daily as an antithromotic, calcium carbonate 2.5 g three times daily from 14Oct2014 as phosphorus binding, pantoprazole 40 mg once daily from 11Nov2016 for heartburn, levothyroxine sodium (THYROXIN) 150 ug once daily for hypothyreosis, paracetamol 1 g as needed for fever and pain, pramipexol 0.088 mg as needed from 08Aug2016 for Restless legs, rosuvastatin 20 mg once daily from 23Feb2005 for hypercholesterolemia, iron (VENOTRIX) 100 mg intravenously weekly from 10Oct2016 as iron supplement, alfacalcidol 1 ug once daily from 10Sep2013 as vitamin D supplementation, ascorbic acid/ biotin/ calcium pantothenate/ folic acid/ nicotinamide/ pyridoxine hydrochloride/ riboflavin/ thiamine mononitrate (RENAVIT) 1 tablet once daily from 10Oct2016 as multivitamin supplementation. There was no baseline blood sample (prior to initiation of epoetin zeta therapy) available for antibody testing. The subject was not exposed to any other erythropoietin (ESA). The subject was hospitalized from 04Nov2016 to 04Nov2016. The subject experienced lack of efficacy with onset date of 08Nov2016, serious due to hospitalization. The reaction was not life-threatening. Relevant test data included, hematocrit 25% on 01Sep2016, 21% on 02Sep2016, 26% on 11Sep2016, 24% on 11Sep2016, 19% on 12Sep2016, 24% on 13Sep2016, 27% on 14Sep2016, 26% on 17Sep2016, 25% on 18Sep2016, 27% on 25Sep2016, 29% on 30Sep2016, 24% on 10Oct2016, 24% on 11Oct2016, 25% on 13Oct2016, 31% on 18Oct2016, 23% on 27Oct2016, 19% on 03Nov2016, 22% on 04Nov2016, 23% on 05Nov2016, 22% on 08Nov2016; and hemoglobin 79 g/l and 80 g/l, on an unspecified dates, 82 g/l on 01Sep2016, 67 g/l on 02Sep2016, 85 g/l on 11Sep2016, 81 g/l on 11Sep2016, 64 g/l on 12Sep2016, 78 g/l on 13Sep2016, 89 g/l on 14Sep2016, 84 g/l on 17Sep2016, 82 g/l on 18Sep2016, 89 g/l on 25Sep2016, 96 g/l on 30Sep2016, 80 g/l on 10Oct2016, 79 g/l on 11Oct2016 and 13Oct2016, 99 g/l on 18Oct2016, 78 g/l on 27Oct2016, 62 g/l on 03Nov2016, 73 g/l on 04Nov2016 and 05Nov2016, and 71 g/l on 08Nov2016. Epoetin zeta dose was increased but due to the lack of efficacy, it was withdrawn and another ESA was started thereafter. The outcome of the event was unknown. The event was considered unrelated to the study drug.

Follow-up (09Dec2016): New information received from the investigator: updating of therapy stop date,action taken in response to the event and confirmation of causality.

Amendment: This follow-up report is being submitted to amend previously reported information: subject's gender is male not female.

Case Comment: On the basis of the available information, the Company considered it's possible that the epoetin zeta therapy was ineffective in treating renal anemia. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-SEP-2016	Blood calcium	0.92 mmol/l/pH 7.4	
2	02-SEP-2016	Blood calcium	0.98 mmol/l/pH 7.4	
3	13-SEP-2016	Blood calcium		
4	14-SEP-2016	Blood calcium	0.81 mmol/l/pH 7.4	
5	16-SEP-2016	Blood calcium	0.81 mmol/l/pH 7.4	
6	17-SEP-2016	Blood calcium	0.81 mmol/l/pH 7.4	
7	18-SEP-2016	Blood calcium	0.86 mmol/l/pH 7.4	
8	19-SEP-2016	Blood calcium	0.90 mmol/l/pH 7.4	
9	20-SEP-2016	Blood calcium	0.87 mmol/l/pH 7.4	
10	22-SEP-2016	Blood calcium	0.91 mmol/l/pH 7.4	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
11	23-SEP-2016	Blood calcium	0.94 mmol/l/pH 7.4	
12	25-SEP-2016	Blood calcium	0.89 mmol/l/pH 7.4	
13	30-SEP-2016	Blood calcium	0.93 mmol/l/pH 7.4	
14	07-OCT-2016	Blood calcium	0.87 mmol/l/pH 7.4	
15	10-OCT-2016	Blood calcium	0.78 mmol/l/pH 7.4	
16	13-OCT-2016	Blood calcium	0.97 mmol/l/pH 7.4	
17	18-OCT-2016	Blood calcium	1.16 mmol/l/pH 7.4	
18	27-OCT-2016	Blood calcium	1.01 mmol/l/pH 7.4	
19	03-NOV-2016	Blood calcium	0.94 mmol/l/pH 7.4	
20	02-SEP-2016	Blood parathyroid hormone	319 ng/l	
21	10-OCT-2016	Blood parathyroid hormone	295 ng/l	
22	27-OCT-2016	Blood parathyroid hormone	244 ng/l	
23	02-SEP-2016	Blood phosphorus	1.65 mmol	
24	14-SEP-2016	Blood phosphorus	1.89 mmol	
25	15-SEP-2016	Blood phosphorus	1.68 mmol	
26	17-SEP-2016	Blood phosphorus	1.58 mmol	
27	18-SEP-2016	Blood phosphorus	1.57 mmol	
28	19-SEP-2016	Blood phosphorus	1.66 mmol	
29	20-SEP-2016	Blood phosphorus	1.61 mmol	
30	23-SEP-2016	Blood phosphorus	1.60 mmol	
31	26-SEP-2016	Blood phosphorus	1.73 mmol	
32	30-SEP-2016	Blood phosphorus	2.14 mmol	
33	10-OCT-2016	Blood phosphorus	2.52 mmol	
34	18-OCT-2016	Blood phosphorus	1.14 mmol	
35	27-OCT-2016	Blood phosphorus	1.00 mmol	
36	03-NOV-2016	Blood phosphorus	1.25 mmol	

Mfr. Control Number: 2016557897

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
37	01-SEP-2016	C-reactive protein	6 mg/l	
38	11-SEP-2016	C-reactive protein	58 mg/l	
39	11-SEP-2016	C-reactive protein	28 mg/l	
40	12-SEP-2016	C-reactive protein	147 mg/l	
41	13-SEP-2016	C-reactive protein	151 mg/l	
42	14-SEP-2016	C-reactive protein	105 mg/l	
43	15-SEP-2016	C-reactive protein	136 mg/l	
44	16-SEP-2016	C-reactive protein	127 mg/l	
45	17-SEP-2016	C-reactive protein	91 mg/l	
46	18-SEP-2016	C-reactive protein	66 mg/l	
47	19-SEP-2016	C-reactive protein	62 mg/l	
48	20-SEP-2016	C-reactive protein	53 mg/l	
49	21-SEP-2016	C-reactive protein	38 mg/l	
50	22-SEP-2016	C-reactive protein	31 mg/l	
51	23-SEP-2016	C-reactive protein	25 mg/l	
52	26-SEP-2016	C-reactive protein	18 mg/l	
53	30-SEP-2016	C-reactive protein	8 mg/l	
54	10-OCT-2016	C-reactive protein	<3 mg/l	
55		Haematocrit	%	
56	01-SEP-2016	Haematocrit	25 %	
57	02-SEP-2016	Haematocrit	21 %	
58	11-SEP-2016	Haematocrit	24 %	
59	11-SEP-2016	Haematocrit	26 %	
60	12-SEP-2016	Haematocrit	19 %	
61	13-SEP-2016	Haematocrit	24 %	
62	14-SEP-2016	Haematocrit	27 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
63	17-SEP-2016	Haematocrit	26 %	
64	18-SEP-2016	Haematocrit	25 %	
65	25-SEP-2016	Haematocrit	27 %	
66	30-SEP-2016	Haematocrit	29 %	
67	10-OCT-2016	Haematocrit	24 %	
68	11-OCT-2016	Haematocrit	24 %	
69	13-OCT-2016	Haematocrit	25 %	
70	18-OCT-2016	Haematocrit	31 %	
71	27-OCT-2016	Haematocrit	23 %	
72	03-NOV-2016	Haematocrit	19 %	
73	04-NOV-2016	Haematocrit	22 %	
74	05-NOV-2016	Haematocrit	23 %	
75	08-NOV-2016	Haematocrit	22 %	
76		Haemoglobin	79 g/l	
77		Haemoglobin	80 g/l	
78	01-SEP-2016	Haemoglobin	82 g/l	
79	02-SEP-2016	Haemoglobin	67 g/l	
80	11-SEP-2016	Haemoglobin	85 g/l	
81	11-SEP-2016	Haemoglobin	81 g/l	
82	12-SEP-2016	Haemoglobin	64 g/l	
83	13-SEP-2016	Haemoglobin	78 g/l	
84	14-SEP-2016	Haemoglobin	89 g/l	
85	17-SEP-2016	Haemoglobin	84 g/l	
86	18-SEP-2016	Haemoglobin	82 g/l	
87	25-SEP-2016	Haemoglobin	89 g/l	
88	30-SEP-2016	Haemoglobin	96 g/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
89	10-OCT-2016	Haemoglobin	80 g/l	
90	11-OCT-2016	Haemoglobin	79 g/l	
91	13-OCT-2016	Haemoglobin	79 g/l	
92	18-OCT-2016	Haemoglobin	99 g/l	
93	27-OCT-2016	Haemoglobin	78 g/l	
94	03-NOV-2016	Haemoglobin	62 g/l	
95	04-NOV-2016	Haemoglobin	73 g/l	
96	05-NOV-2016	Haemoglobin	73 g/l	
97	08-NOV-2016	Haemoglobin	71 g/l	
98	11-NOV-2016	Reticulocyte count	2.8 %	
99	12-NOV-2016	Reticulocyte count	2 %	
100	10-OCT-2016	Serum ferritin	670 microg/l	
101	05-NOV-2016	Serum ferritin	440 microg/l	
102	08-AUG-2016	Transferrin	1.67 g/l	
103	10-OCT-2016	Transferrin	1.92 g/l	
104	05-NOV-2016	Transferrin	1.77 g/l	
105	08-AUG-2016	Transferrin saturation	27 %	
106	10-OCT-2016	Transferrin saturation	29 %	
107	05-NOV-2016	Transferrin saturation	28 %	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	10000 IU every 3rd day; Intravenous	renal anemia (Nephrogenic anaemia)	11-OCT-2016 / 08-NOV-2016; 29 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) PENICILLIN /00000901/ (BENZYLPENICILLIN) ; 26-SEP-2016 / 18-OCT-2016

#8) DALTEPARINE SODIQUE (DALTEPARIN SODIUM) ; 12-SEP-2016 / Unknown

#9) LISPRO INSULIN (INSULIN LISPRO) ; Unknown

Mfr. Control Number: 2016557897

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#10) CEFTRIAXONE (CEFTRIAXONE) ; 11-SEP-2016 / 16-NOV-2016

#11) ASA (ACETYLSALICYLIC ACID) ; Unknown

#12) CALCIUM CARBONATE (CALCIUM CARBONATE) ; 14-OCT-2014 / Unknown

#13) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 11-NOV-2016 / Unknown

#14) THYROXIN (LEVOTHYROXINE SODIUM) ; Unknown

#15) PARACETAMOL (PARACETAMOL) ; Unknown

#16) PRAMIPEXOL (PRAMIPEXOLE DIHYDROCHLORIDE) ; 08-AUG-2016 / Unknown

#17) ROSUVASTATIN (ROSUVASTATIN) ; 23-FEB-2005 / Unknown

#18) PRAZOSIN (PRAZOSIN) ; 16-NOV-2016 / Unknown

#19) VENOTRIX (IRON) ; 10-OCT-2016 / Unknown

#20) ALPHACALCIDOL (ALFACALCIDOL) ; 10-SEP-2013 / Unknown

#21) RENAVIT (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHENATE, FOLIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE MONONITRATE) ; 10-OCT-2016 / Unknown

#22) INSULIN DETEMIR (INSULIN DETEMIR) ; 10-FEB-2016 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypothyreosis (Hypothyroidism);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	07	AUG	1935	80 Years	Male	69.50 kg	04	APR	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

transient ischemic attack [Transient ischaemic attack]

Case Description: EPOE-09-11: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, Protocol EPOE-09-11, regarding subject 0940023.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 4SO22T4}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) S. renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 21-SEP-2015 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
29-NOV-2008 to Ongoing	Relevant Med History	Terminal renal insufficiency (End stage renal disease)
10-DEC-2003 to Unknown	Relevant Med History	Bladder cancer (Bladder cancer)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2016562333

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-FEB-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 80-year-old Caucasian male subject started to receive epoetin zeta (RETACRIT) (lot # 4SO22T4), 3000 IU twice weekly, administered subcutaneously, on 21Sep2015 for renal anemia. The last dose of study drug before the event was on 04Apr2016. Main dosage 1 was on 08Feb2016 for hemoglobin of 9.9 g/dl. Main dosage 2 was on 07Mar2016 for hemoglobin 10.3 g/dl. The subject's medical history included terminal renal insufficiency since 29Nov2008 with hemodialysis and polyneuropathy since 22Sep2008, both ongoing, bladder tumor since 10Dec2003, prostate cancer since 17Dec1999, depression since 23Jul2015, carpal tunnel syndrome since Nov2015, thigh amputation in 1954, and apoplexy. Concomitant medication was unknown. Erythropoietin-stimulant medications the subject received in the past included methoxy polyethylene glycol-epoetin beta (MIRCERA) 150 mg from 24Nov2010 to 19Jan2011 with hemoglobin 11.3 g/dl on 08Nov2010 and 13.1 g/dl on 10Jan2011; and epoetin theta (EPORATIO) 2000 IU from 14Feb2012 to 12Sep2012 with an unspecified hemoglobin on 12Mar2012 and 11.1 g/dl on 10Sep2012. No episodes of lack of efficacy/ deficient response, and no development of anti-erythropoietin antibodies (AEB) during treatment with other erythropoietin stimulants. Dialysis protocol was performed on 08Feb2016 and 07Mar2016. Tests for the last 3 months prior to event included hemoglobin 9.1 on 11Jan2016, 9.9 on 08Feb2016, 10.3 on 07Mar2016 (normal range: 13, 5-17.8 g/dl); hematocrit 29% on 11Jan2016, 32% on 08Feb2016, 33% on 07Mar2016 (normal range: 40-53%); erythrocytes 3.0 on 11Jan2016, 3.4 on 08Feb2016, 3.6 on 07Mar2016 (normal range: 4.4-5.9 Mio/µl); leucocytes 8.1 on 11Jan2016, 6.7 on 08Feb2016, 8.0 on 07Mar2016 (normal range 3.7-9.9 Tsd/µl); C-reactive protein (CRP) unspecified result on 11Jan2016, 4.47 on 08Feb2016, 3.39 on 07Mar2016 (normal range 0-0.50 mg/dl); calcium 1.93 on 11Jan2016, 2.0 on 08Feb2016, 1.90 on 07Mar2016 (normal range 2.15-2.58); phosphate 3.26 on 11Jan2016, 3.22 on 08Feb2016, 2.64 on 07Mar2016 (normal range 2.5-4.5 mg/dl). On 04Apr2016, dialysis protocol was performed and the subject experienced a transient ischemic attack and was hospitalized. "After drowsiness initial, today recurring speech production, word finding" Hemoglobin was 6.1. The subject received 2 packs of erthrocytes (concentrates). "Gastrointestina-diagnosticl, motor aphasia, father aopplex". This was clarified as this wording was extracted from the hospital records for information of other medical colleagues. The subject was hospitalized on 04Apr2016 with suspicion of apoplex, with word finding problems, the hemoglobin (Hb) was 6.1 and the subject received two erythrocyte concentrates. As reported on 10Feb2017, this was a comment in the dialysis protocol from the treating physician on 06Apr2016 as internal information for himself and other physicians. The subject was still hospitalized since the evening of 04Apr2016. The subject was admitted to hospital-neurology. No special action was taken with the study drug in response to the event. The subject was considered to have recovered from the transient ischemic attack on 19Apr2016. He was discharged from the hospital on an unspecified date. The investigator reported that there was not a reasonable possibility that the event, transient ischemic attack, was related to treatment with epoetin zeta or to a concomitant medication.

Follow-up (14Jan2017): New information received from the contactable investigator included: study drug details, medical history, past drug history, subject's details, action taken

Follow-up (10Feb2017): Updates hospitalization data, treatment data, test data, and event data.

Case Comment: In agreement with the investigator, the Company considered that there was not a reasonable possibility that the event, transient ischemic attack, was related to treatment with epoetin zeta. The subject has major thromboembolic risk factors including underlying malignancy. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	04-APR-2016	Haemoglobin	6.1	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
17-DEC-1999 to Unknown	Relevant Med History	Prostate cancer (Prostate cancer);
22-SEP-2008 to Ongoing	Relevant Med History	Polyneuropathy (Polyneuropathy);
23-JUL-2015 to Unknown	Relevant Med History	Depression (Depression);
NOV-2015 to Unknown	Relevant Med History	Carpal tunnel syndrome (Carpal tunnel syndrome);
1954 to Unknown	Relevant Med History	Amputation above knee (Leg amputation);
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
Unknown	Family History	Apoplexy (Cerebrovascular accident);
24-NOV-2010 to 19-JAN-2011	Past Drug Event	Mircera (MIRCERA);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	150 mg	
14-FEB-2012 to 19-SEP-2012	Past Drug Event 2000 IU	eporatio (EPORATIO);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1938	79 Years	Male	79.00 kg	07	FEB	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Bleeding intracerebral [Cerebral haemorrhage]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a non-interventional study report from the observational study, protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 3000 IU, 1x/week	#1) Unknown

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-JUL-2015 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) MARCUMAR (PHENPROCOUMON) ; AUG-2014 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
20-DEC-2012 to Ongoing	Relevant Med History	Terminal renal insufficiency (End stage renal disease)
25-MAR-2015 to Ongoing	Relevant Med History	Dialysis (Dialysis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017064895

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-MAR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 79-year-old male subject started epoetin zeta (RETACRIT) 3000 units per week on 21Jul2015, then 10000 units twice weekly on 11Aug2016 for the study indication of renal anemia. The subject's medical history included terminal renal insufficiency since 20Dec2012, extracorporeal dialysis since 25Mar2015, insulin dependent diabetes mellitus type 2 since 1990, all ongoing; prostate cancer on 07Jan2013, arterial hypertension, and atrial fibrillation. Concomitant medications included phenprocoumon (MARCUMAR) since the beginning of Aug2014 due to chronic atrial fibrillation. It was reported that on 10Jan2017 the subject had pain with slight confusion and disorientation; decreased liver profile. On 07Jun2017, it was clarified that most likely it was headache. Unfortunately, it cannot be said exactly since the indication of pain localization had not been documented. Additionally, on 07Jun2017 it was reported that confusion and disorientation were not considered early signs of a cerebral bleeding but as signs of worsening of general condition, accompanied by the indicated pain. The subject was hospitalized on 08Feb2017 for an intracerebral bleed. The event was reported as bleeding intracerebral with an onset date of 07Feb2017. The subject had a hemorrhage in the basal ganglion area on the left. It was reported that the subject was soporous during the further stationary course and showed a motor hemisyndrome on the right. Test data included calcium of 2.41 on 12Jan2017, phosphate of 3.39 on 12Jan2017, potassium of 4.2 on 12Jan2017, blood pressure of 150/90 and 140/80 on 07Jan2017, blood pressure (arterial/venous) of -117/107 mmhg on 07Jan2017, -140/90 mmhg on 10Jan2017 and -85/102 mmhg on 12Jan2017, blood flow of 350 ml/min on 07Jan2017, 300 ml/min on 10Jan2017 and 320 ml/min on 12Jan2017, C-reactive protein of 1.80 on 12Jan2017, hemoglobin A1C of 6.5 on 12Jan2017, hemoglobin of 11.7 g/dl on 10Jan2017 and 11 g/dl on 13Jan2017, international normalized ratio (INR) of 2.0 on 12Jan2017, ferritin of 423 on 12Jan2017, and body weight of 74.1 kg on 07Jan2017, 77.6 kg on 10Jan2017 and 77.3 kg on 12Jan2017. Additional tests included, on 07Feb2017, ALT was 17 IU/l, albumin globulin ratio 1.09, alpha 1 globulin 6.5%, alpha 2 globulin 9.4%, AST 22 IU/l, beta 2 globulin 7.2%, beta 1 5%, albumin electroph. i.s 52.1%, blood alkaline phosphatase 120 IU/l, bilirubin 0.75 mg/dl, blood lactate dehydrogenase 202 IU/l, gamma-GT 20 IU/l, gamma globulin i.S. 18.8%, INR >6, protein in serum 6.8 g/dl, Quick's test 6. A control several hours following inpatient admission showed an INR of 1.24 and on the following day 1.10. It was reported that epoetin zeta was permanently withdrawn in response to the event with the last dose taken on 07Feb2017. The outcome of the event was unknown. Current results and outcome are not available as the subject is no longer treated in the practice. The subject had left the hospital on 20Feb2017 in a very bad general condition. After discharge, all medical measures were refused by his relatives according to the subject's wish. It was reported that the subject was discontinued from the study as the study criteria was no longer fulfilled. The investigator reported that there was not a reasonable possibility that the event, bleeding intracerebral, was related to the study drug or any concomitant medications.

Amendment: This follow-up report is being submitted to amend previously reported information: drug name updated in narrative to be epoetin zeta.

Follow-up (23Feb2017 and 25Feb2017): Updates epoetin zeta dose details, study details regarding discontinuation, action taken, test data, treatment, event causality and event details.

Follow-up (24Apr2017): Follow-up attempts completed. No further information expected.

Follow-up (07Jun2017): Updates event onset date, reaction data, test data.

Follow-up (26Jun2017): Updates subject status, hospitalization dates

Follow-up (28Mar2019): Updates subject's age.

Follow-up attempts completed. No further information expected.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the event "bleeding intracerebral" was related to study drug epoetin zeta therapy. However, the Company considered that concomitant anticoagulant therapy with phenprocoumon (with increased INR >6) provided the most likely explanation towards the reported event. The underlying conditions including arterial hypertension were deemed as significant risk factors as well.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-FEB-2017	Alanine aminotransferase	17 IU/l	49
2	07-FEB-2017	Albumin globulin ratio	1.09	2.20 1.30
3	07-FEB-2017	Alpha 1 globulin	6.5 %	4.9 2.9
4	07-FEB-2017	Alpha 2 globulin	9.4 %	11.8 7.1
5	07-FEB-2017	Aspartate aminotransferase	22 IU/l	49
6	07-FEB-2017	Beta 2 globulin	7.2 %	6.5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				3.5
7	07-FEB-2017	Beta globulin	5.0 %	7.2 4.7
8	07-FEB-2017	Blood albumin	52.1 %	66.1 55.8
9	07-FEB-2017	Blood alkaline phosphatase	120 IU/l	130 40
10	07-FEB-2017	Blood bilirubin	0.75 mg/dl	1.2 0.1
11	12-JAN-2017	Blood calcium	2.41	
12	07-FEB-2017	Blood lactate dehydrogenase	202 IU/l	249 0
13	12-JAN-2017	Blood phosphorus	3.39	
14	12-JAN-2017	Blood potassium	4.2	
15	07-JAN-2017	Blood pressure measurement	-117/107 mmHg	
16	07-JAN-2017	Blood pressure measurement	150/90	
17	07-JAN-2017	Blood pressure measurement	140/80	
18	10-JAN-2017	Blood pressure measurement	-140/90 mmHg	
19	12-JAN-2017	Blood pressure measurement	-85/102 mmHg	
20	07-JAN-2017	Blood test	350 ml/min	
21	10-JAN-2017	Blood test	300 ml/min	
22	12-JAN-2017	Blood test	320 ml/min	
23	12-JAN-2017	C-reactive protein	1.80	
24	07-FEB-2017	Electrophoresis protein		
25	07-FEB-2017	Gamma-glutamyltransferase	20 IU/l	59
26	12-JAN-2017	Glycosylated haemoglobin	6.5	
27	10-JAN-2017	Haemoglobin	11.7 g/dl	
28	13-JAN-2017	Haemoglobin	11 g/dl	
29	07-FEB-2017	Immunoglobulins	18.8 %	18.8
30	12-JAN-2017	International normalised ratio	2.0	1.0 0.8
31	07-FEB-2017	International normalised ratio	>6.0	1.0 0.8
32	08-FEB-2017	International normalised ratio	1.24	1.0 0.8

Mfr. Control Number: 2017064895

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33	09-FEB-2017	International normalised ratio	1.10	1.0 0.8
34	07-FEB-2017	Protein total	6.8 g/dl	8.3 6.6
35	07-FEB-2017	Prothrombin time	6.0 %	80
36	12-JAN-2017	Serum ferritin	423	
37	07-JAN-2017	Weight	74.1 kg	
38	10-JAN-2017	Weight	77.6 kg	
39	12-JAN-2017	Weight	77.3 kg	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	10000 IU, 2x/week; Unknown	Renal anemia (Nephrogenic anaemia)	11-AUG-2016 / 07-FEB-2017; 181 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1990 to Ongoing	Relevant Med History	Insulin-requiring type 2 diabetes mellitus (Insulin-requiring type 2 diabetes mellitus);
07-JAN-2013 to Unknown	Relevant Med History	Prostate cancer (Prostate cancer);
Unknown	Relevant Med History	Hypertension arterial (Hypertension);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1925	91 Years	Male	95.00 kg	13	JAN	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

media infarction cardioembolic [Embolic stroke]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11. This 91-year-old male subject, received epoetin zeta (RETACRIT) 2000 IU subcutaneously every 2 weeks from 08May2014 and ongoing for renal anemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, every 2 weeks	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 08-MAY-2014 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Adipositas (Obesity)
Unknown	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017073945

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-OCT-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included adipositas, hypertension, and atrial fibrillation. It was reported that the subject had no concomitant medications. On 13Jan2017, the subject suffered from media infarction cardioembolic that required hospitalization from 13Jan2017 to 18Jan2017. The subject did not receive any treatment for the event. Dose was not changed in the last 3 months prior to the event. No basic value for antibody tests were available. The subject never received erythropoetin stimulated agents. Risk for thromboembolic events: adipositas. The subject did not smoke, had no current surgeries, traumas, short-term weight changes, no immobilisation. It was unknown if the subject had factor V Leiden, protein C or S deficiency, antithrombin G20210A mutation, homocystein anemia, positive family history. No other risks were known. Tests included: neutrophils 70.06 % on 14Dec2012 (normal range: 41-70), lymphocytes 20.64 % on 14Dec2012 (normal range: 22-48), creatinine 1.44 mg/dl on 01Sep206 and 1.48 mg/dl on 07Nov2016 (normal range: 0.7-1.2), uric acid 8.38 mg/dl on 01Sep2016 and 7.84 mg/dl on 07Nov2016 (normal range: 3.6-8.2), hemoglobin 11.6 g/dl on 01Sep206 and 12.4 g/dl on 07Nov2016 (normal range: 13-18), hematocrit 42% on 01Sep2016 and 37.9% on 07Nov2016 (normal range: 39-54); erythrocytes 3.16/pl on 01Sep2016 and 3.43/pl on 07Nov2016 (normal range: 4.2-6.2), mean cell volume (MCV) 112.2 fl on 01Sep2016 and 110.5 fl on 07Nov2016 (normal range: 83-97). No action was taken with epoetin zeta in response to the event. The subject recovered with sequelae (dysarthria) on 17Jan2017. The investigator reported that there was not a reasonable possibility that the event, cardioembolic media infarction, was related to epoetin zeta or any concomitant medications.

Follow-up (01Mar2017): Updates subject's details, study drug start date, treatment details

Follow-up (20Mar2017): Updates medical history, test data, adds additional information.

Follow-up (18Oct2019): Update to subject's year of birth.

Case Comment: Investigator's causality opinion is noticed, however Company considers that there was a reasonable possibility that the reported event "media infarction cardioembolic" is related to epoetin zeta therapy based on the known increased risk of thromboembolic events. Additional information including clinical event details and diagnostic tests results is required for a comprehensive assessment of the case. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-SEP-2016	Blood creatinine	1.44 mg/dl	1.2 0.7
2	07-NOV-2016	Blood creatinine	1.48 mg/dl	1.2 0.7
3	01-SEP-2016	Blood uric acid	8.38 mg/dl	8.2 3.6
4	07-NOV-2016	Blood uric acid	7.84 mg/dl	8.2 3.6
5	01-SEP-2016	Haematocrit	42 %	54.0 39.0
6	07-NOV-2016	Haematocrit	37.9 %	54.0 39.0
7	01-SEP-2016	Haemoglobin	11.6 g/dl	18 13
8	07-NOV-2016	Haemoglobin	12.4 g/dl	18 13
9	14-DEC-2012	Lymphocyte count	20.64 %	48 22
10	01-SEP-2016	Mean cell volume	112.2 fl	97 83
11	07-NOV-2016	Mean cell volume	110.5 fl	97 83
12	14-DEC-2012	Neutrophil count	70.06 %	70 41
13	01-SEP-2016	Red blood cell count decreased	3.16/pl	6.2 4.2
14	07-NOV-2016	Red blood cell count decreased	3.43/pl	6.2 4.2

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	25	FEB	1928	88 Years	Female	53.00 kg	10	OCT	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

pelvic vein thrombosis [Pelvic venous thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a non-interventional study report for Protocol EPOE-09-11, regarding subject 048038.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 3000 IU, 3x /week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 11-APR-2016 / Ongoing

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SIMVASTATIN (SIMVASTATIN) ; Unknown
#2) TRAMAL LONG (TRAMADOL HYDROCHLORIDE) ; Unknown
#3) PANTOZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Unknown
#4) BISOPROLOL (BISOPROLOL) ; Unknown
#5) DEKRISTOL (COLECALCIFEROL) ; Unknown
#6) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHE

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Axial hiatal hernia (Hiatus hernia)
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017082349

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-MAR-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 88-year-old Caucasian female subject started treatment with epoetin zeta (RETACRIT) subcutaneously 3000 IU subcutaneously three times weekly since 11Apr2016 for the study indication of renal anemia. Dose was given on 01Jul2016, with hemoglobin on that day 11.6 g/dl, and on 08Aug2016, with hemoglobin 11.6 g/dl. The dose was not changed in the last 3 months before the event. The subject's medical history included hypertension arterial, renal insufficiency stage 4 of unknown origin, peritoneal dialysis, suspected hypertensive-vascular impairment with differential diagnosis of atrophic kidneys on both sides, secondary hyperparathyroidism, metabolic acidosis, condition after hip TEP, condition after pancreatitis, rheumatoid arthritis (polyarthrosis of the finger joints) since 1959, condition after appendectomy, condition after herniotomy on the right, hyperlipidemia since May2016, hypertonia since 2005, suspected early gastric carcinoma since Jun2016, moderate chronic slightly active erosive HP negative antrum gastritis since Jun2016, sling ablation of 4 tubulo-villous structured adenomas with low intraepithelial neoplasia of the colon since Jun2016, and condition after perianal discharge of blood most likely due to a non-irritated pandiverticulosis, all ongoing, condition after cholecystectomy, and big axial hiatal hernia without signs of a reflux esophagitis. The subject did not experience any thromboembolic events upon erythropoietin treatment. The subject did not suffer from following conditions: ischemic heart disease, transient ischemic attack, peripheral artery closure, diabetes mellitus, atrial fibrillation, diarrhea. The subject did not have any of the following risk factors: adiposity, smoking, factor V problems, protein C or S deficiency, anti-thrombin III deficiency, prothrombin G20210A mutation, homocysteine anemia, recent surgeries, trauma, significant and rapid changes in the body weight as a result of water retention or excretion, blood vessels abnormality, aneurysm, immobilization, recent pregnancy or positive family history. Her concomitant medications included simvastatin 20 mg once daily, tramadol hydrochloride (TRAMAL LONG) once daily, pantoprazole sodium sesquihydrate (PANTOZOL) 40 mg once daily, bisoprolol 0.5 once daily, colecalciferol (DEKRISTOL) 0.5 once a week on Wednesday), ascorbic acid/ biotin, calcium pantothenate/ folic acid/ nicotinamide/ pyridoxine hydrochloride/ riboflavin/ thiamine hydrochloride (DREISAVIT-N), alfacalcidolone (ONE ALPHA) once a day five times a week (off on Saturday and Sunday), iron 100 mg once daily by mouth, sodium bicarbonate (NEPHROTRANS) 40 mg twice daily (not with meals), phenprocoumon (MARCUMAR) according to INR, and an unspecified product "RESTORIC POWDER" (a dietary product for additional enriched nutrition - high calories and protein) once daily. The subject received no erythropoietin stimulating products. The investigator reported the subject was hospitalized due to suspicion of thrombosis. Examination revealed a pelvic vein thrombosis. The event was reported as pelvic vein thrombosis, considered serious for hospitalization with an onset date of 10Oct2016. As the subject suffers of a gastric cancer the thrombosis seems to correlate with the cancer as a paraneoplastic event. Anticoagulation therapy was started. Resection of the cancer was not possible by minimal invasive procedures; the subject refused any operation. The following details were provides as per the hospital discharge letter (printed 21Oct2016). The subject was hospitalized from 10Oct2016 to 20Oct2016. Diagnoses: (1) Pelvic vein thrombosis on the right (differential diagnosis paraneoplastic genesis; currently oral anticoagulation therapy with Marcumar paused - currently bridging with heparin perfusion; prescription of compression tights of class II); (2) Suspected early gastric carcinoma (first diagnosed in Jun2016; currently macroscopic suspected progress with polypoid mucosa pre-pyloric towards the angle; intestinal metaplasia pre-pyloric (histopathologic with formations of a highly differentiated adenocarcinoma (G1) of mucosa type, intestinal type according to Lauren, currently basically similar to Jun2016); permanent highly dosed proton pump inhibition (PPI); currently transfer for endosonography and if necessary mucosa ectomy in another hospital on 20Oct2016; (3) Currently Helicobacter pylori (H.P.) negative pangastritis, most likely gastritis of type C (condition after moderately chronic, slightly active erosive H. P. negative antrum gastritis with regenerate epithelium formations (Jun2016); (4) Currently urinary tract infection with Citrobacter freundii (oral antibiosis with Ciprofloxacin); (5) Big axial hiatal hernia without signs of a reflux esophagitis; (6) Sling ablation of 4 tubulo-villous structured adenomas with low intraepithelial neoplasia of the colon in Jun2016 (complete removal partly histomorphologically not provable, no further examinations recommended); (7) Arterial hypertension (known suspicion of a beginning hypertensive heart disease; (8) Renal insufficiency stage 4 of unknown origin (peritoneal dialysis on Sunday/Tuesday/ Thursday; suspected hypertensive-vascular impairment with differential diagnosis of atrophic kidneys on both sides; peritoneal dialysis as nightly intermittent peritoneal dialysis since Mar2016; renal anemia; secondary hyperparathyroidism; known metabolic acidosis); (9) Condition after hip TEP (total endoprothesis); (10) Condition after pancreatitis; (11) Rheumatoid arthritis (first diagnosed in 1959; polyarthrosis of the finger joints); (12) Condition after cholecystectomy; (13) Condition after appendectomy; (14) Condition after herniotomy on the right; and (15) Condition after peranal discharge of blood, most likely due to a non-irritated pan-diverticulosis in Jun2016 (normocytic, normochromic anemia, most likely due to bleeding; differential diagnosis renal anemia; renunciation of a further diagnostic investigations). Anamnesis: Admittance via nephrology: enlargement of scope and pain in the right leg. Last in-patient stay in same hospital in Jun2016; peranal discharges of blood most likely within due to a nonirritated pan-diverticulosis. Since 2 days existing painful swelling of the right leg according to self anamnesis of patient. Physical examination: blood pressure 156/84 mmHg, pulse 82/ min, temperature 36.3 degrees C, breathing rate 15/min, oxygen saturation 93%, satisfying general condition and good nutritional condition, awake, responsive and orientated, hypacusis (hearing devices are at home), obvious swelling of the complete right leg up to the groin, hematoma on the right (bruised), no redness, no hyperthermia, heart arrhythmic with normal frequency, clear heart tones, lung on both sides ventilated equally with vesicular breathing sound, abdomen soft without tenderness on palpation and active vermicular movement, peritoneal dialysis catheter prone left lower abdomen. Compression sonography right leg: pelvic vein thrombosis on the right (consultation with vascular surgery: no vascular surgery intervention, conservative therapy). Laboratory parameters were not provided. ECG: sinus rhythm, heart rate 80/min, left type, S-persistence up to V6, no significant disturbances of repolarization. X-ray (10Oct2016): slim medium-sized heart. Minimal streaky growth of the drawing at the right upper surface presumably due to calloused genesis. No pre-recordings available. No distinct pneumonia, no round lesions, no effusion or congestion. Assessment: no clear acute pathology can be detected. Abdomen sonography, duplex sonography of the pelvic- limb veins (12Oct2016): normal size of liver with sharp margin and smoothly limited. The liver hepatic reflex pattern is homogeneously hypoechoic. No evidence of focal liver lesions. Normal liver vessel image. The inferior vena cava is normal-calibrated and properly perfused. The right iliac vein is not compressible up to the bifurcation and is not perfused in the color duplex. The left iliac vein is free. The urinary bladder is fluid-filled and smoothly limited. The corpus uteri is not enlarged. No evidence of a pathological intestinal cockade. Minimal residual diluent fluid in the small pelves. Pancreas size is normal large. The gall bladder is absent. The DHC

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(ductus hepatocholedochus) with 3 mm is in the standard range. The abdominal aorta is sclerosing and normal wide. The stems of the celiac trunk are also markedly sclerosed. The spleen is of normal size. Both kidneys with 7 cm shrunk with an echo wealthy narrow parenchyma edge and closed central reflex. Assessment: Known pelvic venous thrombosis on the right, V.cava inferior (VCI) is free, iIntraabdominally no tumor detection, Condition after cholecystectomy with normal wide DHC, significant abdominal aortic sclerosis without ectasia, known shrinkage of the kidneys with residual dialysis liquid in the small pool, no urinary retention, low volume status with colloiding VCI, upper abdominal sonography without findings. Gastroscopy:
esophagus-gastro-duodenoscopy/histology of the upper intesinal tract (13Oct2016): inserting the endoscope with sight, regular mucosal results in the area of the tubular esophagus. Z-line lining on the diaphragm, strictly limited, sparsely clear secretion on an empty stomach, at the inversion dot-shaped erythema at fundus and cardia, corpus mucosal folds relief regular with dot-shaped erythema, peristalsis regular, in the antrum dot-shaped erythema, prepyloric white mucosa as seen in intestinal metaplasia with polypoid mucosa changes (sample taking), especially towards the angulus fold, with suspicion of progression of the Jun2016 diagnosed early gastric carcinoma, pylorus is decurved, slightly gaping, ordinary mucosa finding in bulbus duodeni as well as descending duodenum. Diagnosis: pangastritis; suspicion of progression of the above-mentioned gastric carcinoma with polypoid mucosa prepyloric especially towards the angulus folds, sample taking; intestinal metaplasia prepyloric; otherwise regular esophagus-gastro-duodenoscopy. Histopathology: gastric mucosa biopsy from clinical prepyloric with formations of a highly differentiated adenocarcinoma (G1) of the mucosa type: intestinal type after Lauren. It is a matter of a fundamentally similar histologic picture as in the previous results. Nephrological council (17Oct2016): Findings: patient with new pelvic venous thrombosis (paraneoplastic?), effective anticoagulation needed, peritoneal dialysis with remaining renal function of 6.5 ml/min. With suspicion of gastric carcinoma an endosonography is planned, with mucosectomy if necessary. Assessment: With the newly deep venous thrombosis is a safe effective anticoagulation with Clexane not clearly controllable. Better would be a bridging with Heparin intravenous and partial thromboplastin time (PPT) monitoring. If an earlier inpatient admission is impossible I recommend Clexane 1x40 sc (subcutaneous) and factor Xa-monitoring. Diagnosis: Deep venous thrombosis and early gastric carcinoma. Summary and course: Inpatient admission of the patient happened because of the above mentioned symptoms. Duplex sonography showed the diagnosis of a pelvic venous thrombosis right side. With the previously known finding of a well differentiated gastric adenocarcinoma with suspicion of an early gastric carcinoma (first diagnosed Jun2016), as mentioned above in the findings, a paraneoplastic genesis cannot be excluded. With the previously known end-stage renal insufficiency and dependence on peritoneal dialysis we initially started an effective anticoagulation with Heparin perfusion. Before starting oral anticoagulation treatment with Marcumar a gastroscopic control took place resulting in the above mentioned findings. Currently macroscopy showed mostly likely a progression of the gastric carcinoma, first diagnosed in June this year. A further diagnosis and treatment at suspicion to gastric carcinoma was initially unwanted by the patient. After renewed consultation the patient and her relatives desire further treatment. Regarding this we recommend further endosonographic diagnosis with if applicable mucosectomy if early gastric carcinoma is suspected. For this we introduced the patient to another hospital. Lately we paused the newly initiated oral anticoagulation treatment with Marcumar and continued a bridging in the context of anticoagulation through Heparin perfusion. A urinary tract infection with proof of Citrobacter freundii was treated antibiotically orally with a renal adapted dosage with Ciprofloxacin. We kindly request to control the urinary status over time. Because of the first diagnosis of a pelvic venous thrombosis right we prescribe the patient compression tights (class 2), which we be delivered to the patients house throughout. Until then, the here given, temporary preoperative support stocking shall be worn. The patient is already receiving a mobile nursing service twice a day. This service will ambulantly undertake the daily application of the compression tights. A prescription for this was issued and given to the patient. Due to lately slight haemoglobin decrease with no sign to a currently active hemorrhage we are asking kindly for a control of the small blood count (hemogram) in a timely manner. Because of a current deficiency of iron while marginal yet normal serum-ferritin we started an oral iron substitution. As we discussed the relocation of the patient to the endsonographic examination with if applicable mucosectomy is happening today. We are pausing the current anticoagulation with Heparin perfusion for this on the 20Oct2016 at 4 am. Furthermore the oral anticoagulation should be continued over the long term with Marcumar as discussed with the supervising general doctor. Informing for the pending endosonographic investigation took place already. Discharge medications: Simvastatin 20mg (0-0-1); tramadol hydrochloride (TRAMAL) long 200 mg (1-0-0); pantoprazole sodium sesquihydrate (PANTOZOL) 40 mg (0-0-1); Bisoprolol 5mg (0.5-0-0); ascorbic acid/ biotin/ calcium pantothenate/ folic acid/ nicotinamide/ pyridoxine hydrochloride/ riboflavin/ thiamine hydrochloride DREISAVIT) N (1-0-0); colecalciferol (DEKRISTOL) 20.000 IU (0.5-0-0, 1x/week, on Wednesdays); Restoric powder (1-0-0); alfacalcidol (ONE ALPHA) 0,5 (1-0-0, 5x/week, off on Saturday and Sunday); Iron 100mg oral (1-0-0); sodium bicarbonate (NEPHROTRANS) 840mg (1-0-1 (not with meals)); phenprocoumon (MARCUMAR) (according to INR, currently paused); Heparin-Perfusion (controlled via PTT, goal 40-80). Additional tests included erythrocytes 3.78 x10^6/mm3 on 14Jun2016 (normal range 3.9-5.2); hemoglobin 10.6 g/dl on 02Mar2017, 10.6 g/dl on 16Feb2017, 11 g/dl on 06Feb2017, 11 g/dl on 03Jan2017, 10.9 g/dl on 06Dec2016, 10.1 g/dl on 08Nov2016, 11.1 g/dl on 01Nov2016, 9.8 g/dl on 03May2016 (normal range 11.2- 15.7); hematocrit 34 % on 16Feb2017, 32.7 % on 08Nov2016, 31.6 % on 03May2016 (normal range 34.1-44.9); MCH 25.3 pg on 02Mar2017, 25.2 pg on 16Feb2017, 25.1 pg on 06Dec2016, 25.3 pg on 08Nov2016, 32.3 pg on 03May2016 (normal range 25.6-32.2); MCHC: 30.4 g/dl on 02Mar2017, 31.2 g/dl on 16Feb2017, 30.6 g/dl on 03Jan2017, 29.5 g/dl on 06Dec2016, 30.9 g/dl on 08Nov2016, 31.1 g/dl on 04Oct2016, 30.6 g/dl on 01Sep2016, 31 g/dl on 03May2016 (normal range 32.0-36.0); thrombocytes 460 x10 3/mm3 on 08Nov2016, 25.3 x10 3/mm3 on 02Mar2017, 25.2 x10 3/mm3 on 16Feb2017, 25.1 x10 3/mm3 on 06Dec2016, 25.3 x10 3/mm3 on 08Nov2016, 32.3 x10 3/mm3 on 03May2016 (normal range 150-400); transferrin saturation 10.6 % on 03Jan2017 (normal range 16.0-45.0). No action was taken with the study drug in response to the event. The subject was considered to be recovering from the event. The investigator reported the event of pelvic vein thrombosis was unrelated to the study medication and concomitant drugs.

Follow-up (10Mar2017): Updates medical history, study drug details

Follow-up: (20Mar2017): Updates medical history, tests

Case Comment: Investigator causality opinion is noticed, however Company considered that there was a reasonable possibility that the use of epoetin zeta may have favored the onset of event "pelvic vein thrombosis" in this elderly female patient based on temporal

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

association and the known increased risk of thromboembolic events. Underlying malignancy was considered as contributory factor as well. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	03-MAY-2016	Basophilia	1.0 %	1.0
2	07-JUN-2016	Basophilia	1.0 %	1.0
3	02-JUL-2016	Basophilia	1.0 %	1.0
4	01-SEP-2016	Basophilia	1.0 %	1.0
5	16-FEB-2017	Basophilia	1.2 %	1.0
6	02-MAR-2017	Basophilia	1.1 %	1.0
7	OCT-2016	Blood pressure measurement	156/84 mmHg mmHg	
8	OCT-2016	Body temperature	36.3 Centigrade	
9	OCT-2016	Electrocardiogram	Sinus rhythy, Heart rate 80/min, left type, S-pers	
10	07-JUN-2016	Eosinophil count	6.8 %	6.0 1.0
11	03-MAY-2016	Haematocrit	31.6 %	44.9 34.1
12	08-NOV-2016	Haematocrit	32.7 %	44.9 34.1
13	16-FEB-2017	Haematocrit	34 %	44.9 34.1
14	03-MAY-2016	Haemoglobin	9.8 g/dl	15.7 11.2
15	01-JUL-2016	Haemoglobin	11.6 g/dl	15.7 11.2
16	02-AUG-2016	Haemoglobin	11.6 g/dl	15.7 11.2
17	01-NOV-2016	Haemoglobin	11.1 g/dl	15.7 11.2
18	08-NOV-2016	Haemoglobin	10.1 g/dl	15.7 11.2
19	11-NOV-2016	Haemoglobin	10.4 g/dl	15.7 11.2
20	06-DEC-2016	Haemoglobin	10.9 g/dl	15.7 11.2
21	03-JAN-2017	Haemoglobin	11 g/dl	15.7 11.2
22	06-FEB-2017	Haemoglobin	11 g/dl	15.7 11.2
23	16-FEB-2017	Haemoglobin	10.6 g/dl	15.7 11.2
24	02-MAR-2017	Haemoglobin	10.6 g/dl	15.7 11.2
25	OCT-2016	Heart rate	82	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
26	03-MAY-2016	Mean cell haemoglobin	32.3 pg	32.2 25.6
27	08-NOV-2016	Mean cell haemoglobin	25.3 pg	32.2 25.6
28	06-DEC-2016	Mean cell haemoglobin	25.1 pg	32.2 25.6
29	16-FEB-2017	Mean cell haemoglobin	25.2 pg	32.2 25.6
30	02-MAR-2017	Mean cell haemoglobin	25.3 pg	32.2 25.6
31	03-MAY-2016	Mean cell haemoglobin concentration	31 g/dl	36.0 32.0
32	01-SEP-2016	Mean cell haemoglobin concentration	30.6 g/dl	36.0 32.0
33	04-OCT-2016	Mean cell haemoglobin concentration	31.1 g/dl	36.0 32.0
34	08-NOV-2016	Mean cell haemoglobin concentration	30.9 g/dl	36.0 32.0
35	06-DEC-2016	Mean cell haemoglobin concentration	29.5 g/dl	36.0 32.0
36	03-JAN-2017	Mean cell haemoglobin concentration	30.6 g/dl	36.0 32.0
37	16-FEB-2017	Mean cell haemoglobin concentration	31.2 g/dl	36.0 32.0
38	02-MAR-2017	Mean cell haemoglobin concentration	30.4 g/dl	36.0 32.0
39	03-MAY-2016	Mean cell volume	10.43E-08 ul	9.48E-08 7.94E-08
40	07-JUN-2016	Mean cell volume	9.84E-08 ul	9.48E-08 7.94E-08
41	14-JUN-2016	Mean cell volume	9.68E-08 ul	9.48E-08 7.94E-08
42	02-JUL-2016	Mean cell volume	9.49E-08 ul	9.48E-08 7.94E-08
43	02-AUG-2016	Monocyte count	13.9 %	13.0 5.0
44	04-OCT-2016	Monocyte count	13.6 %	13.0 5.0
45	17-OCT-2016	Nephrological examination	deep venous thrombosis, early gastric carcinoma	
46	13-OCT-2016	Oesophagogastroduodenoscopy	pangastritis, suspected progress of gastric carcin	
47	OCT-2016	Oxygen saturation	93 %	
48	03-MAY-2016	Platelet count	32.3 x10 3/mm3	400 150

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
49	08-NOV-2016	Platelet count	25.3 x10 3/mm3	400 150
50	08-NOV-2016	Platelet count	460 x10 3/mm3	400 150
51	06-DEC-2016	Platelet count	25.1 x10 3/mm3	400 150
52	16-FEB-2017	Platelet count	25.2 x10 3/mm3	400 150
53	02-MAR-2017	Platelet count	25.3 x10 3/mm3	400 150
54	03-MAY-2016	Red blood cell scan	3 x10 6/mm3	5.2 3.9
55	14-JUN-2016	Red blood cell scan	3.78 x10 6/mm3	5.2 3.9
56	OCT-2016	Respiratory rate	15	
57	03-JAN-2017	Transferrin saturation	10.6 %	45 16
58	12-OCT-2016	Ultrasound Doppler	Known pelvic venous thrombosis on the right, V.cav	
59	OCT-2016	Ultrasound scan	pelvic vein thrombosis on the right	
60	10-OCT-2016	X-ray	no clear acute pathology can be detected	

13. Relevant Tests

ECG (10Oct2016-20Oct2016): sinus rhythm, heart rate 80/min, left type, S-persistence up to V6, no significant disturbances of repolarization.
X-ray (10Oct2016): slim medium-sized heart. Minimal streaky growth of the drawing at R upper surface presumably due to calloused genesis. No pre-recordings available. No distinct pneumonia, no round lesions, no effusion or congestion.
Abdomen sonography, duplex sonography of pelvic limbs (12Oct2016): normal size of liver with sharp margin & smoothly limited. Liver hepatic reflex pattern is homogeneously hypoechoic. No evidence of focal liver lesions. Normal liver vessel image. Inferior vena cava is normal-calibrated & properly perfused. R iliac vein is not compressible up to the bifurcation & is not perfused in the color duplex. L iliac vein is free. Urinary bladder is fluid-filled & smoothly limited. The corpus uteri is not enlarged. No evidence of pathological intestinal cockade. Minimal residual diluent fluid in small pelves. Pancreas size is normal large. Gall bladder is absent. The DHC with 3 mm is in the standard range. Abdominal aorta is sclerosing & normal wide. The stems of the celiac trunk are also markedly sclerosed. The spleen normal large. Both kidneys with 7 cm shrunk with a echo wealthy narrow parenchyma edge and closed central reflex.
Gastroscopy: esophagus-gastro-duodenoscopy/histology of the upper GI (13Oct2016): Histology: gastric mucosa biopsy from clinical prepyloric with formations of a highly differentiated adenocarcinoma (G1) of the mucosa type: intestinal type after Lauren. It is a matter of a fundamentally similar histologic picture as in the previous results.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#6) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHENATE, FOLIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) ; Unknown

#7) ONE ALPHA (ALFACALCIDOL) ; Unknown

#8) IRON (IRON) ; Unknown

#9) NEPHROTRANS (SODIUM BICARBONATE) ; Unknown

#10) MARCUMAR (PHENPROCOUMON) ; Unknown

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History Stage 4 of unknown origin	Renal insufficiency (Renal failure);
Unknown to Ongoing	Relevant Med History SUN/TUES/THURS, as nightly intermittent PD since Mar2016	Peritoneal dialysis (Peritoneal dialysis);
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy);
Unknown to Ongoing	Relevant Med History	Hyperparathyroidism secondary (Hyperparathyroidism secondary);
Unknown to Ongoing	Relevant Med History	Metabolic acidosis (Metabolic acidosis);
Unknown to Ongoing	Relevant Med History	Hip total replacement (Hip arthroplasty);
Unknown to Ongoing	Relevant Med History	Pancreatitis (Pancreatitis);
1959 to Ongoing	Relevant Med History polyarthrosis of the finger joints	Rheumatoid arthritis (Rheumatoid arthritis);
Unknown	Relevant Med History	Cholecystectomy (Cholecystectomy);
Unknown to Ongoing	Relevant Med History	Appendectomy (Appendicectomy);
Unknown to Ongoing	Relevant Med History	Herniotomy (Hernia repair);
MAY-2016 to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
2005 to Ongoing	Relevant Med History	Hypertonia (Hypertonia);
JUN-2016 to Ongoing	Relevant Med History stomach early carcinoma	Gastric carcinoma (Gastric cancer);
JUN-2016 to Ongoing	Relevant Med History	Chronic gastritis (Chronic gastritis);
JUN-2016 to Ongoing	Relevant Med History	Colon neoplasia (Colon neoplasm);
JUN-2016 to Ongoing	Relevant Med History	Adenoma (Adenoma benign);
JUN-2016 to Ongoing	Relevant Med History	Diverticulosis of colon with hemorrhage (Diverticulum intestinal haemorrhagic);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	06	OCT	1931	80 Years	Male	80.00 kg	27	JUL	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

iliac artery occlusion right leg [Iliac artery occlusion]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a non-interventional study report from the observational study, protocol EPOE-09-11, regarding subject |GE115-0045.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, once weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 22-DEC-2011 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPINE (AMLODIPINE) ; Ongoing
#2) CIPROLEX (CIPROFLOXACIN HYDROCHLORIDE) ; Ongoing
#3) DIGIMERCK (DIGITOXIN) ; Ongoing
#4) VALSARTAN (VALSARTAN) ; Ongoing
#5) SIMVASTATIN (SIMVASTATIN) ; Ongoing
#6) MARCUMAR (PHENPROCOUMON) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
OCT-2012 to Unknown	Relevant Med History due to glomerulonephritis	Dialysis (Dialysis)
Unknown	Relevant Med History	Glomerulonephritis (Glomerulonephritis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017095389

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-MAR-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 80-year-old Caucasian male subject started epoetin zeta (RETACRIT) administered 2000 IU subcutaneously once weekly, on 22Dec2011 for the study indication of renal anemia. There have not been any dose changes within three months prior to the event. The subject's medical history included dialysis since Oct2012 due to glomerulonephritis, apoplexy in 2005, in 2008, and in 2010, and peripheral artery occlusive disease of legs ongoing since Mar2010 with bypass in Mar2010, hyperlipidemia, hypertension, and atrial fibrillation. Furthermore, the subject did not suffer from ischemic heart disease, a transient ischemic attack (TIA), diabetes mellitus, diarrhea, cancer, nor any chronic gastrointestinal disorders. The subject did not receive pre-dialysis. Concomitant medications included amlodipine, ciprofloxacin hydrochloride (CIPROLEX), digitoxin (DIGIMERCK), valsartan, simvastatin, and phenprocoumon (MARCUMAR); all ongoing. The subject was not exposed to any other erythropoietin-stimulating agent (ESA) at any time. The subject did not experience any episode of lack of efficacy/ lack of response or any other thromboembolitic event during treatment with any other ESA. The subject did not develop anti-erythropoietin antibodies (AEB) during treatment with any other ESA. On 27Jul2012, the subject suffered an iliac artery occlusion in the right leg, which required hospitalization on the same date. Leg ischemia of the right leg developed despite phenprocoumon therapy though, it was not considered that the event was a consequence of lack of efficacy of phenprocoumon. The cause leading to the event was unknown. Hemoglobin was 10.7 g/dl on 19Apr2012 and 9.7 g/dl on 27Jul2012 (normal range 12-16). Additional tests on 27Jul2012 included chloride 100.9 mmol (95-105), blood gas analysis sodium 135 mmol (134-150), blood gas analysis BE -2.8 mmol, blood gas analysis PH 7.35, blood gas analysis potassium 5.5 mmol (3.6-5.3), CRP 13.81 mg/l (normal range <5), hematocrit 31.7% (36-47), erythrocyte 3.89 (3.9-5.4). It was reported that there was no data available regarding reticulocytes or blood sedimentation rate, ECG, echocardiography, Troponin I and T, creatinine kinase, angiography, cranial computerized tomography (CT), cranial nuclear magnetic resonance imaging (MRT), transcranial Doppler, blood pressure, neurological examination, D-dimer, lung scan, angiography, thorax (CT or MRT), duplex and doppler sonography y or DVT (deep vein thrombosis). Treatment was reported as "femoralis TEA and y-plasty A. fem. profunda." No action was taken with epoetin zeta in response to the event. The subject recovered from the event on 11Aug2012 and was discharged from the hospital on the same date. The event was assessed as unrelated to epoetin zeta.

Follow-up (20Mar2017): Updates subject data, action taken with epoetin zeta, medical history, test data, and event details.

Follow-up (27Mar2017): Updates subject's details, medical history

Case Comment: Based on the follow-up information received and in agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event, iliac artery occlusion, was related to the use of epoetin zeta but most likely due to underlying peripheral artery occlusive disease of legs. Hemoglobin level was not high. The event occurred ten months after the initiation of epoetin zeta and was recovering when epoetin zeta was ongoing. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	27-JUL-2012	Blood chloride	100.9 mmol/l	105 95
2	27-JUL-2012	Blood chloride	100.9 mmol	105 95
3	27-JUL-2012	Blood gases	135 mmol	150 134
4	27-JUL-2012	Blood gases	-2.8 mmol	
5	27-JUL-2012	Blood gases	7.35	
6	27-JUL-2012	Blood gases	5.5 mmol	5.3 3.6
7	27-JUL-2012	C-reactive protein increased	13.81 mg/l	<5.0
8	27-JUL-2012	Haematocrit	31.7 %	47 36
9	19-APR-2012	Haemoglobin	10.7 g/dl	16 12
10	27-JUL-2012	Haemoglobin	9.7 g/dl	16 12
11	27-JUL-2012	Red blood cell count	3.89	5.4 3.9

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2008 to Unknown	Relevant Med History	Apoplexy (Cerebrovascular accident);
2005 to Unknown	Relevant Med History	Apoplexy (Cerebrovascular accident);
2010 to Unknown	Relevant Med History	Apoplexy (Cerebrovascular accident);
MAR-2010 to Ongoing	Relevant Med History of legs; bypass Mar2010	Peripheral arterial occlusive disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	01	JAN	1950	67 Years	Male	74.00 kg	01	FEB	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Cardiopulmonary arrest [Cardio-respiratory arrest]
Sepsis [Sepsis]
Cerebrovascular insult [Cerebrovascular accident]
Bronchopneumonia [Pneumonia]
Urinary tract infection [Urinary tract infection]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 03-APR-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 28-OCT-2014 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) REPAGLINIDE (REPAGLINIDE) ; Ongoing
#2) CORDIPIN XL (NIFEDIPINE) ; Ongoing
#3) TONOCARDIN (DOXAZOSIN) ; Ongoing
#4) FOLACIN (FOLIC ACID) ; Ongoing
#5) NEXIUM (ESOMEPRAZOLE MAGNESIUM) ; Ongoing
#6) ATORVOX (ATORVASTATIN CALCIUM) ; Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2005 to Ongoing	Relevant Med History PCI LAD + stenting x2 2006	Myocardial infarction (Myocardial infarction)
1998 to Ongoing	Relevant Med History type 2	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017097815

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-JUN-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(PASCO II)

This is a report from a non-interventional study, Protocol EPOE-09-11, regarding subject CR0050007. This 67-year-old Caucasian male subject started epoetin zeta (RETACRIT) (batch number: 6Q019Q6) 2000 IU subcutaneously once weekly on 28Oct2014 for renal anemia. Epoetin zeta mean dose 1 on 15Nov2016: 81.1 U/kg/w (frequency: 3 x week) with hemoglobin 124 g/l; mean dose 2: from 26Nov2016 epoetin zeta holiday with hemoglobin 122 g/l on 15Dec2016. The subject received 2000 IU subcutaneously three times a week from 23Sep2016 to 21Oct2016, then 2000 IU once a week from 24Oct2016 to 26Nov2016. There were dose changes within 3 months prior to event: date of change 26Nov2016, new dose: epoetin zeta holidays, hemoglobin prior to dose change: 124 g/l, hemoglobin after dose change: 122 g/l on 15Dec2016. The last dose prior to the event was 26Nov2016. Epoetin zeta was not readministered; instead the subject received blood transfusions when needed. He was treated by doctors in the neurology department and ICU doctors. The subject's medical history included diabetes mellitus and arterial hypertension since 1998, hyperlipidemia since 2000, all ongoing; and a myocardial infarction in 2005 with a percutaneous coronary intervention (PCI) to the left anterior descending (LAD) + stenting x2 in 2006, hemodialysis since 2007, peripheral arterial disease (PAD), diabetic vascular disease, amputation on both legs, and chronic renal failure. Concomitant medications included repaglinide 1 mg, 2 daily for diabetes; nifedipine (CORDIPIN XL) 40 mg daily, doxazosin (TONOCARDIN) 4 mg daily, trandolapril (GOPTEN) 2 mg daily, and urapidil (EBRANTIL) 60 mg, 2 daily, all 4 for hypertension; folic acid (FOLACIN) 5 mg daily when on dialysis for anemia, esomeprazole magnesium (NEXIUM) 20 mg daily for gastritis, atorvastatin calcium (ATORVOX) 10 mg daily for hyperlipidemia, pregabalin (LYRICA) 150 mg, 2 daily for diabetic neuropathy, and ticlopidine hydrochloride (TAGREN) 250 mg daily for anti-aggregation therapy, all taken orally and all ongoing. The patient's past drug history included epoetin beta (NEORECORMON) from Aug2007 to Oct2014 at 162 IU/kg/week with haemoglobin 98 g/l. The subject did not experience any thromboembolic event during treatment with any other ESA. He did not have any of the risk factors: obesity (BMI 22.84 kg/m2), smoking, coagulation disorders, recent surgery, trauma, weight changes, vascular anomalies, aneurysm, immobilization, or positive family history. On 01Feb2017, the subject was admitted to the neurology department due to weakness of his right side. On 01Feb2017, a thorax x-ray was non-significant. Brain MSCT scans on 01Feb2017 and 06Feb2017 found no fresh ischemia or hemorrhagic lesions. MSCT brain: done native, showed infratentorial central and normally wide 4; ventricle with normal structure of cerebellum; supratentorial third ventricle is central, laterals are symmetric and normally wide; in pons and left thalamus old lacunar lesions were present; periventricular, hypoperfusion changes were visible; no new ischemia, hemorrhage, expansion or extraaxial collections were visible; bones were intact. Control MSCT brain: infratentorial central and normally wide 4; ventricle with normal radio morphology of cerebellum was present; supratentorial third ventricle was central and wider with symmetric and wider lateral ventricles; basal cisterns, Sylvian fissure and sulcus of convex hemispheres were wider due to atrophic changes; in right pons and left thalamus lacunar lesions; periventricular, in the white matter of cerebrum hypodense area of chronic, hypoperfusion changes were visible; no new ischemia, hemorrhage, or intracranial expansion were visible; bones were intact. On 07Feb2017 an ultrasound Doppler was non-significant. On 10Feb2017, an electroencephalogram (EEG) was non-significant. A color Doppler (ultrasound) (CDFI) of the carotid arteries on an unspecified date was without significant stenosis. Transcranial Doppler on unspecified date showed blood flow within the circle of Willis on the left is limited while is normal on the other side. Other lab tests included: banded neutrophils 1.0% on 09Feb2017 and 0.0% on 13Feb2017; basophils 0.0% on 13Feb2017 and on 23Feb2017; blood glucose 8.3 on 01Feb2017; C-reactive protein (CRP) 8.1 on 01Feb2017, 59.1 on 09Feb2017, 110.9 on 13Feb2017, 105.7 on 16Feb2017, 92.0 on 21Feb2017, and 75.7 on 23Feb2017; eosinophils 9.0% on 09Feb2017, 2.0% on 13Feb2017, and 5.0% on 23Feb2017; hematocrit 0.295 on 01Feb2017 and 0.268 on 09Feb2017; lymphocytes 14.0% on 09Feb2017, 19.0% on 13Feb2017 and 11.0% on 23Feb2017; monocytes 9.0% on 09Feb2017, 2.0% on 13Feb2027 and 5.0% on 23Feb2017; segmented neutrophils 67.0% on 09Feb2017, 77.0% on 13Feb2017 and 79.0% on 23Feb2017; erythrocytes 3.25 on 01Feb2017, 3.02 on 09Feb2017; and leucocytes 7.1 x10 9/l on 09Feb2017, 8.8 x10 9/l on 13Feb2017 and 9.2 x10 9/l on 23Feb3017; hemoglobin concentrations on 01Feb2017: 96 g/l, 09Feb2017: 90 g/l, 02Mar2017: 60 g/l, 04Mar2017: 101 g/l, 07Mar2017: 92 g/l, 12Mar2017: 89 g/l, 16Mar2017: 80 g/l, 20Mar2017: 95 g/l, 22Mar2017: 89 g/l, 24Mar2017: 103 g/l, and 01Apr2017: 89 g/l. In the discharge letter summary, a neurologic examination showed the subject was hospitalized due to acute, ischemic cerebrovascular insult. Brain MSCT showed lacunar lesions in right pons and left thalamus. Periventricular, in the white matter of cerebrum hypodense area of chronic, hypoperfusion changes were visible. CDFI of carotids without any significant stenosis. During hospitalization, the subject had stable general condition and was discharged with good overall condition. The final diagnosis for this hospitalization was insultus vascularis cerebri and hemiparesis lat.dex. The event was reported as cerebrovascular insult with the onset date of 01Feb2017. The subject was treated with anti-aggregation therapy, low molecular heparin, antihypertensive drugs, gastroprotective drugs, hypolipemic drugs, infusions, and other symptomatic therapy. Treatment was complicated with bronchopneumonia on 09Feb2017 and a urinary tract infection on 13Feb2016, considered serious for hospitalization and important medical events, for which the subject received antibiotic treatment. The subject was discharged from hospital on 25Feb2017 and considered to have recovered from bronchopneumonia and urinary tract infection and recovered with sequelae (unspecified) from cerebrovascular insult all on the same date. On 02Mar2017 during hemodialysis, a cardiac arrest occurred. On the monitor, ventricular tachycardia was observed. The event was reported as cardiopulmonary arrest. Cardio-pulmonary resuscitation (CPR) was performed and the subject was admitted to the intensive care unit (ICU). Lab test indicated elevated HS troponin I. As of 05Mar2017, the subject was still in the ICU and had not yet recovered from the cardiac arrest/ ventricular tachycardia. During the hospitalization in the ICU, the subject developed sepsis on 10Mar2017. His condition deteriorated and he died on 03Apr2017. The cause of death was reported as cardiopulmonary arrest and sepsis which was not determined by autopsy. Sepsis was confirmed by tests: BAL (10Mar2017): Acinetobacter baumanii 10 x 6 CFU/ml, Proteus mirabilis 10 x 4 CFU/ml, Staphylococcus aureus 10 x 5 CFU/ml; Haemoculture (10Mar2017): positive for Klebsiella pneumonia ESBL, Proteus mirabilis Haemoculture (27Mar2017): positive for Acinetobacter baumanii, Pseudomonas aeruginosa Haemoculture (28Mar2017): positive for Pseudomonas aeruginosa, Proteus mirabilis, Acinetobacter baumannii. Cardiopulmonary arrest and sepsis were considered serious for death, life-threatening, hospitalization and important medical events. The investigator reported that there was not a reasonable possibility that the events, cerebrovascular insult cardiopulmonary arrest, bronchopneumonia, urinary tract

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

infection, sepsis, are related to the study medication or to any concomitant medications.

Follow-up (15Mar2017): Updates seriousness criteria, hospital admission date, final diagnosis and treatment for event cardiac arrest/ventricular tachycardia, adds epoetin zeta batch number, suspect drug details, updates medical history, concomitant medications (dosages), lab data and event outcome.

Follow-up (24May2017): Adds death details, tests, study drug details.

Follow-up (09Jun2017): Event term updated to cardiopulmonary arrest from cardiac arrest/ ventricular tachycardia, seriousness updated; new events bronchopneumonia, urinary tract infection, sepsis; event details, tests

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported events were related to epoetin zeta. Advanced age, pre-existing conditions of diabetes mellitus, arterial hypertension and hyperlipidemia were considered as significant risk factors to the development of cerebrovascular insult. The complicated events of bronchopneumonia, urinary tract infection and sepsis were infectious in nature. Cardiopulmonary arrest was most likely due to the patient's underlying/ concurrent conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09-FEB-2017	Band neutrophil count	1.0 %	
2	13-FEB-2017	Band neutrophil count	0.0 %	
3	13-FEB-2017	Basophil count	0.0 %	
4	23-FEB-2017	Basophil count	0.0 %	
5	10-MAR-2017	Blood culture	Klebsiella pneumonia ESBL, Proteus mirabilis	
6	27-MAR-2017	Blood culture	Acinetobacter baumanii, Pseudomonas aeruginosa	
7	28-MAR-2017	Blood culture	Pseudomonas aeruginosa, Proteus mirabilis, Acineto	
8	01-FEB-2017	Blood glucose	8.3	
9		Body mass index	22.84	
10	10-MAR-2017	Bronchoalveolar lavage	positive	
11	01-FEB-2017	C-reactive protein	8.1	
12	09-FEB-2017	C-reactive protein	59.1	
13	13-FEB-2017	C-reactive protein	110.9	
14	16-FEB-2017	C-reactive protein	105.7	
15	21-FEB-2017	C-reactive protein	92.0	
16	23-FEB-2017	C-reactive protein	75.7	
17	01-FEB-2017	Chest X-ray	non significant	
18	01-FEB-2017	Computerised tomogram head	non significant	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
19	06-FEB-2017	Computerised tomogram head	non significant	
20	10-FEB-2017	Electroencephalogram	non significant	
21	09-FEB-2017	Eosinophil count	9.0 %	
22	13-FEB-2017	Eosinophil count	2.0 %	
23	23-FEB-2017	Eosinophil count	5.0 %	
24	01-FEB-2017	Haematocrit	0.295	
25	09-FEB-2017	Haematocrit	0.268	
26		Haemoglobin	98 g/l	
27	15-NOV-2016	Haemoglobin	124 g/l	
28	15-DEC-2016	Haemoglobin	122 g/l	
29	01-FEB-2017	Haemoglobin	96 g/l	
30	09-FEB-2017	Haemoglobin	90 g/l	
31	02-MAR-2017	Haemoglobin	60 g/l	
32	04-MAR-2017	Haemoglobin	101 g/l	
33	07-MAR-2017	Haemoglobin	92 g/l	
34	12-MAR-2017	Haemoglobin	89 g/l	
35	16-MAR-2017	Haemoglobin	80 g/l	
36	20-MAR-2017	Haemoglobin	95 g/l	
37	22-MAR-2017	Haemoglobin	89 g/l	
38	24-MAR-2017	Haemoglobin	103 g/l	
39	01-APR-2017	Haemoglobin	89 g/l	
40	09-FEB-2017	Lymphocyte count	14.0 %	
41	13-FEB-2017	Lymphocyte count	19.0 %	
42	23-FEB-2017	Lymphocyte count	11.0 %	
43	09-FEB-2017	Monocyte count	9.0 %	
44	13-FEB-2017	Monocyte count	2.0 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
45	23-FEB-2017	Monocyte count	5.0 %	
46	09-FEB-2017	Neutrophil count	67.0 %	
47	13-FEB-2017	Neutrophil count	77.0 %	
48	23-FEB-2017	Neutrophil count	79.0 %	
49	01-FEB-2017	Red blood cell count	3.25	
50	09-FEB-2017	Red blood cell count	3.02	
51		Troponin I	elevated	
52		Ultrasound Doppler	non significant	
53	07-FEB-2017	Ultrasound Doppler	non significant	
54	09-FEB-2017	White blood cell count	7.1 x10 9/l	
55	13-FEB-2017	White blood cell count	8.8 x10 9/l	
56	23-FEB-2017	White blood cell count	9.2 x10 9/l	

13. Relevant Tests

BMI (unknown): 22.84 kg/m2
MSCT brain: done native, showed infratentorial central and normally wide 4. ventricle with normal structure of cerebellum. Supratentorial third ventricle is central, laterals are symmetric and normally wide. In pons and left thalamus old lacunar lesions are present. Periventricular, hypoperfusion changes are visible. No new ischaemia, hemorrhage, expansion or extraaxial collections are visible. Bones are intact.
Control MSCT brain: infratentorial central and normally wide 4. ventricle with normal radio morphology of cerebellum is present. Supratentorial third ventricle is central and wider with symmetric and wider lateral ventricles. Basal cisterns, Sylvian fissure and sulcus of convex hemispheres are wider due to atrophic changes. In right pons and left thalamus lacunar lesions. Periventricular, in the white matter of cerebrum hypodense area of chronic, hypoperfusion changes are visible. No new ischaemia, hemorrhage, or intracranial expansion are visible. Bones are intact.
Transcranial Doppler: blood flow within the circle of Willis on the left is limited while is normal on the other side.
Neurological exam (discharge letter summary): the patient was hospitalized due to acute, ischaemic cerebrovascular insult. Brain MSCT showed lacunar lesions in right pons and left thalamus . Periventricular, in the white matter of cerebrum hypodense area of chronic, hypoperfusion changes are visible. CDFI of carotids without any significant stenosis. Treatment was complicated with the bronchopneumonia and urinary tract infection due to the patient received antibiotic treatment. During hospitalization, the patient had stable general condition was discharged with good overall condition.
Bronchoalveolar lavage (10Mar2017): Acinetobacter baumanii 10 x 6 CFU/ml, Proteus mirabilis 10 x 4 CFU/ml, Staphylococcus aureus 10 x 5 CFU/ml,.
Haemoculture (28Mar2017): Pseudomonas aeruginosa, Proteus mirabilis, Acinetobacter baumannii

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	2000 IU, 3x week; Subcutaneous	renal anemia (Nephrogenic anaemia)	23-SEP-2016 / 21-OCT-2016; 29 days

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	2000 IU, weekly; Subcutaneous	renal anemia (Nephrogenic anaemia)	24-OCT-2016 / 26-NOV-2016; 34 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) EBRANTIL (URAPIDIL) ; Ongoing

#8) LYRICA (PREGABALIN) ; Ongoing

#9) TAGREN (TICLOPIDINE HYDROCHLORIDE) ; Ongoing

#10) GOPTEN (TRANDOLAPRIL) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1998 to Ongoing	Relevant Med History	Hypertension arterial (Hypertension);
2000 to Ongoing	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia);
2006 to Unknown	Relevant Med History	Percutaneous coronary intervention (Percutaneous coronary intervention);
2006 to Unknown	Relevant Med History	Stent insertion NOS (Stent placement);
2007 to Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
AUG-2007 to OCT-2014	Past Drug Event dose: 162 IU/kg/w Haemoglobin range: 98 g/l	NeoRecormon (NEORECORMON);
Unknown	Relevant Med History Diabetic vascular disease, amputation on both legs	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Chronic renal failure (Chronic kidney disease);
Unknown	Relevant Med History	Diabetic vascular disorder (Diabetic vascular disorder);
Unknown	Relevant Med History amputation on both legs	Leg amputation (Leg amputation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	GERMANY		OCT	1956	60 Years	Male	74.00 kg	14	NOV	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pulmonary embolism [Pulmonary embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11, regarding subject 0930175.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, 3 per week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 19-JUL-2016 / 12-NOV-2016	#1) 117 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Ongoing
#2) FOLIC ACID (FOLIC ACID) ; Ongoing
#3) L-THYROXIN (LEVOTHYROXINE SODIUM) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
08-JUN-2016 to Ongoing	Relevant Med History	Renal failure (Renal failure)
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017103232

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
02-MAY-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 60-year-old Caucasian male subject, described as not Hispanic or Latino, started epoetin zeta (RETACRIT) 4000 IU 3 times per week on 19Jul2016 for the study indication of nephrogenic anemia. Main dose no.1: 16Aug2016: 12000IU / week, Hemoglobin 9.6g / dl; Main dose no.1: 16Aug2016: not available, Hemoglobin: not available. The dose regimen has not been changed within the last 3 months before the event occurred. No other erythropoietin stimulating medications were administered at any time before the event. The subject's medical history was significant for renal failure since 08Jun2016, hypertension, diabetes, heart failure, and atrial fibrillation, all ongoing. The subject was receiving hemodialysis. The subject had no other thromboembolic event risk factors. Concomitantly, the subject was taking pantoprazole for prophylaxis, folic acid for prophylaxis, and levothyroxine (L-THYROXIN), all taken by mouth and ongoing. The subject was admitted to the hospital on 10Nov2016 for implantation of a dialysis catheter. During the surgery, the subject developed a pulmonary embolism, considered serious due to hospitalization, with an onset date of 14Nov2016. Information provided on hospital discharge letter (hospitalization from 10Nov2016 to 29Dec2016) included:
Diagnosis:
1. Acute right heart decompensation in the presence of lung artery embolism left: occurred during catheter insertion on 14Nov2016. Initially no CT Thorax could be performed due to cardiac instability. Echocardiogram cor pulmonale, good left ventricular functionality. Treatment with Heparin perfusor with PTT goal of 60-70 seconds. Partially catecholamine necessary (noradrenaline and dobutamine). Due to respiratory insufficiency, intubation and ventilation for 10 days, extubation on 24Nov2016, in the further course noninvasive ventilation (NIV) treatment, actually only oxygen administration. Firstly CICA dialysis, in the further course switch on intermitting dialysis, consiliar Demers-catheter insertion on 01Dec2016. CT thorax as of 29Nov2016: surrounded fresh thrombotic parts without complete obstruction in the area of the junction of the segmentoid arteries and lower lobe left, effusion right including compression atelectasis in lower lobe and parts middle lobe, no infiltrates. Punctuation of ascites on 18Nov2016, in the further course switch from heparin to phenprocoumon (MARCUMAR) as applicable. Furthermore intermitting dialysis (3x/week) recommended, limitation of drinking amount.
2. unclear infection, most likely bronchopulmonary. Differential diagnosis: CRP increase, elevated temperature, infect parameters. X -ray could not be taken for determination, CT Thorax not possible due to patient was unstable. Ascites as transudate. Trachea secrete: Candida dubliniensis in low amount of pathogens, typical colonization pathogen under Antibiotic treatment, significant pathogen). Initially treatment with piperacillin/ tazobactam (TAZOBAX), in the course switch on imipenem, under treatment CRP fluctuation in low levels, lastly no fever. In CT Thorax. No evidence of infiltrates. In blood culture up to now no pathogen creation possible.
3. Tachyarrhythmia absoluta in the presence of known atrial fibrillation. Under beta-blocking agents and 3 times administration of digoxin actually normofrequent atrial fibrillation.
4. Leukocytosis and thrombocytosis of unknown recovery. Punctuation recommended.
5. hypochrom microcytary anemia, most likely to be characterized as a 'mixture' with renal insufficiency and leuko-thrombocytosis. Actually light bleeding after Sheldon under heparin perfusor. Today: Hemoglobin at 7.0 mg/dl otherwise between 7.4 and 9.2, Erythrocyte concentrate ordered.
6. Signs of a transportation disturbance in duodenum, performed under a gastrointestinal tube. Fluid level in pars descendens duodeni, otherwise inconspicuous. Initiation of a prokinetic therapy under placement of a trelumina tube. In the further course clinical improvement, then nutritional development.
Preliminary diseases: Occlusion of a lower arm slope shunt right in Sep2016, unclear leukocytosis, terminal dialysis requiring renal insufficiency. Diabetes mellitus type II (insulin dependent), nosocomial basal pneumonia right, arterial hypertension, hypothyroidism. Chronic viral hepatitis type B without Delta Virus, left heart insufficiency, with complaints at rest. Gastroesophageal reflux disease.
Procedures: X-ray of thorax (intensive) as of 14Nov2016, findings: when lying, right heart enlargement, right-sided effusion also into interlobium. Indication on potential infiltration's of lung. Left lung seems to be free.
Echocardiography as of 16Nov2016: Middle up to high graded biatrialc dilatation, systolic function still given, paradox septum movements as a indication of right heart complaint. Not determined: Ascites.
X-ray of thorax (intensive) as of 16Nov2016: increased shadowing in right lower field, unsharp diaphragm crests both sides. State after extubation.
X-ray of thorax (intensive) as of 18Nov2016:Diagnostic and relieving punctuation 5000 ml ascites.
Microbiology of the ascites punctuation as of 18Nov2016. No pathogens could be artificially created, no yeasts could be detected.
X-ray of thorax (intensive) as of 21Nov2016: No change of basic findings, enlarged shadow of heart, right-sided pleural effusion.
Blood tests on 21Nov2016 included: absolute albumin 3.28 g/dl (range 3.5 - 5.5), alkaline phosphatase 156 IU/l (range 40 - 129), creatinine 1.53 mg/dl (range 0.50 - 1.30), parathyroid hormone 114 (range 15 - 65), phosphate 2.3 mg/dl (range 2.5 - 4.5), potassium 5.3 mmol/l (range 3.7 - 5.0), urea 75 mg/dl (range 15 - 46), CRP 3.78 mg/dl (range 0.00 - 0.80), hematocrit 36.7% (range 42 - 52), hemoglobin 9.6 g/dl (range 14 - 18), thrombocytes 647 x10 3/mm3, erythrocytes 4.63 x10 6/mm3, and leucocytes 28.4 x10 3/mm3.
Esophago-Gastro-Duodenoscopy as of 22Nov2016.
Placement of Trelumina tube in pars descendens duodeni, no complications
Therapy Recommendation: Prokinetic therapy, from 23Nov2016 start of enteral nutrition with 500 ml/20 h via duodenal ankle of Trelumina tube. Exclusion of a stenosis in the upper GI area, except a indication of a transportation disturbance in duodenum, no pathological finding.
X-ray of thorax (intensive) as of 24Nov2016: Suspicion of infiltration of right lower field of lung, ventilation disturbance of basal lung areas both sides. No pulmonary venous stasis. No melting coin lesions.
X-ray of thorax (intensive) as of 24Nov2016: No pneumothorax.
X-ray of left upper arm as of 29Nov2016. No evidence of a fracture , inconspicuous joints and parts of thorax.
CT of skull as of 29Nov2016: brain volume decreased including bright inner and outer cerebrospinal fluid spaces, no indication of a circulation disorder, bleeding or dimension claim. No early signs of an infarction. No edema, calcification of ACI in Siphon area. Inconspicuous areas of orbita. No injury of skull. Minor ventilation of both mastoids and tympanon right. Circulary swellings of

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

mucosa in ethmoidal cells and sinus sphenoidalis.
CT of Thorax as of 29Nov2017: surrounded fresh thrombotic parts without complete obstruction in the area of the junction of the segmentoid arteries and lower lobe left. The perfusion in lower lobe is in normal condition. Particularly Truncus pulmonalis and main pulmonary arteries free. Enlarged pleural effusion right sided with compression atelectasis in lower lobe and middle lobe. No extensive pulmonary infiltrates. General cardiac expansion. Increasement of lymph nodes mediastal paraaortal.
Liver and spleen enlargement with significant ascites in upper belly gastrointestinal tube and central line placement left and right jugular.
The patient was orally intubated after hemodynamic and oxygenatoric instability and the hereby non-implementation of the planned insertion of a Demers catheter, medicinal sedated and pressure controlled ventilated transferred to our intensive care unit (initially supervised by our anesthesiology colleagues). At admission, the peripheral measured saturation under increased in - as well as expiratory pressure and a FiO2 of 0,6 100%. The hemodynamic is unstable under continuous, high dosage noradrenalin-infusion as well as low-dosage epinephrine infusion, normal heart rate arrhythmic with chronical persistent atrial fibrillation. Auscultatory bilateral wheezing, abdomen is soft with sonographic detectable ascites perihepatic, extremities are slim, warm, regularly recapillarized. Pupil reactions slow intact. Blood gas analysis showed a strong metabolic acidosis without increased lactate, laboratory chemical a preexisting leukocytosis. Echocardiographic a strong right cardiac dilatation with D-sign and right precordial congestion can be seen, so that as a cause a severe Cor pulmonale /Right-heart decompensation can be assumed. Because of an acute-to-chronical kidney failure a continuous citrate dialysis will be started, the catecholamine therapy will be changed to dobutamine/ noradrenaline. The gas exchange is sufficient, the FiO2 can be lowered to 0,4, the ventilator parameters are unobtrusive. The first try of weaning failed with quickly substantial cough activity and development of a severe bronchus spasm. With elevated infect parameters a calculated antibiotic therapy with Tazobac was initiated. In the further process the catecholamines were able to be reduced stepwise with mean arterial pressure (MAP) over 70 mmHg. Because of the CICA-dialysis subject was able to be clearly negatively balanced.
The chest radiograph increasing signs of congestion, additionally leaking pleural effusion on the right, but echocardiographic good left ventricle (LV)-pumping function, furthermore acute right heart signs of strain presentable. Abdomen sonographic no severe pleura effusion presentable, but evidence of a lot of ascites, so that on the 18Nov2016 a puncture of 5 liter slight bloody discolored ascites took place, here no sign of germs, also no sign of malignant cells.
During the course CRP fluctuating between 3 and 11 mg/dl. With radiological suspicion of infiltrate (not precisely differentiated) and again increasing infection values the antibiotic therapy was changed to Imipenem, with this no increased temperature anymore, CRP furthermore slightly increased. After successful weaning extubating took place on the 24Nov2016, followed by initially non-invasive ventilation (NIV) therapy, during the course transition to intermittent NIV-therapy, with this good blood gas analysis. Finally a good oxygenation with oxygen therapy was able to be reached. In the chest radiograph further evidence of pleura effusion on the right, thereupon the duration of dialysis was prolonged, resulting in improved balance. The patient was overall positively balanced however with completely absent urine production. With the transition from Nutriflex to an oral diet the IV fluid intake was able to be reduced further and in total a negative balance was able to be reached.
For more precise differentiation of the thoracic X-ray results and still unclear increased infection values and a CT thorax with the focus on effusion/infiltrates/lung emboli has been performed to exclude a pulmonary embolism. Here by engulfed fresh thrombus parts at the level of the separation of the segmental arteries to the lower lobes on the left without complete obstruction could be displayed, additionally effusion on the right with compression atelectasis in the lower lobes and middle lobes part - no infiltrates.
The patient got increasingly attentive and showed a significant slurred speech. In the CCT (cranial computer tomography) there has not been a hint at an intracranial bleeding or fresh signs of ischemic.
On the 01Dec2016 a complication-free insertion of a Demers catheter during local anesthesia by our vascular surgery colleagues. The intermittent dialysis should be continued. Also urgent need of restriction of liquid intake!!
In the further process not catecholamine liable anymore. Hemodynamic and respiratory stable. Therefore today we will transfer subject on our station E3.
Medication at transfer: Heparin-perfusor 25 000/50 ml after PTT value, PTT target value 60-70s, pantoprazole 20 mg 1-0-0, folic acid 5 mg1-0-0, levothyroxine 75 µg 1-0-0, ramipril Pause, torasemide (TOREM) Pause, xipamide Pause, sucroferric oxyhydroxide (VELPHORO) Pause. Inhalation with salbutamol and ipratropium (ATROVENT) each 8* four times a day, lorazepam (TAVOR) 0.5 mg if needed (up to three times a day), blood glucose day profile (BZ TP), blood glucose target value: 160 mg/dl, correction factor 30, correction with soluble insulin (ACTRAPID), liquid intake: max. 500 ml. The subject was discharged on 18Jan2017 and transferred to a rehabilitation facility. No action was taken with the study drug in response to the event. The outcome of the event was unknown. The investigator reported that the event, pulmonary embolism, was not related to the study drug or to any concomitant medication.

Follow-up (10Mar2017): Updates subject data (approximate date of birth), action taken, causality with regard to concomitant drugs, test data, and confirms seriousness criterion.

Follow-up (24Apr2017): New information received from the investigator included: subject details, study drug details, medical history, hospitalization dates, event details, treatment, tests

Follow-up (02May2017): Updates tests.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event was related to the study drug Epoetin Zeta. The study drug was started on 19-JUL-2016 and the event occurred on 14-NOV-2016, 118 days later. The event was most likely related to an intercurrent or underlying condition. The follow-up information received does not alter the previous company clinical evaluation.

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	19-JUL-2016	Blood albumin	2.83 g/dl	5.5 3.5
2	21-NOV-2016	Blood albumin	3.28 g/dl	5.5 3.5
3	10-JUN-2016	Blood alkaline phosphatase	270 IU/l	129 40
4	19-JUL-2016	Blood alkaline phosphatase	174 IU/l	129 40
5	16-AUG-2016	Blood alkaline phosphatase	156 IU/l	129 40
6	21-NOV-2016	Blood alkaline phosphatase	156 IU/l	129 40
7	14-FEB-2017	Blood alkaline phosphatase	191 IU/l	129 40
8	20-MAR-2017	Blood alkaline phosphatase	164 IU/l	129 40
9	04-APR-2017	Blood alkaline phosphatase	137 IU/l	129 40
10	19-JUL-2016	Blood calcium	1.99 mmol/l	2.80 2.00
11	10-JUN-2016	Blood creatine	2.61 mg/dl	1.30 0.50
12	19-JUL-2016	Blood creatine	2.44 mg/dl	1.30 0.50
13	16-AUG-2016	Blood creatine	4.54 mg/dl	1.30 0.50
14	21-NOV-2016	Blood creatine	1.53 mg/dl	1.30 0.50
15	14-FEB-2017	Blood creatine	3.44 mg/dl	1.30 0.50
16	20-MAR-2017	Blood creatine	4.8 mg/dl	1.30 0.50
17	04-APR-2017	Blood creatine	4.63 mg/dl	1.30 0.50
18	10-JUN-2016	Blood parathyroid hormone	91.8	65 15
19	19-JUL-2016	Blood parathyroid hormone	63.3	65 15
20	16-AUG-2016	Blood parathyroid hormone	112	65 15
21	21-NOV-2016	Blood parathyroid hormone	114	65 15
22	14-FEB-2017	Blood parathyroid hormone	73.6	65 15
23	20-MAR-2017	Blood parathyroid hormone	39.2	65 15
24	04-APR-2017	Blood parathyroid hormone	59.1	65 15
25	19-JUL-2016	Blood phosphorus	3.9 mg/dl	4.5 2.5
26	16-AUG-2016	Blood phosphorus	6 mg/dl	4.5 2.5
27	21-NOV-2016	Blood phosphorus	2.3 mg/dl	4.5 2.5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
28	14-FEB-2017	Blood phosphorus	6.6 mg/dl	4.5 2.5
29	20-MAR-2017	Blood phosphorus	4 mg/dl	4.5 2.5
30	04-APR-2017	Blood phosphorus	5.1 mg/dl	4.5 2.5
31	10-JUN-2016	Blood potassium	7.2 mmol/l	5.0 3.7
32	19-JUL-2016	Blood potassium	5 mmol/l	5.0 3.7
33	16-AUG-2016	Blood potassium	5.4 mmol/l	5.0 3.7
34	21-NOV-2016	Blood potassium	5.3 mmol/l	5.0 3.7
35	14-FEB-2017	Blood potassium	5.4 mmol/l	5.0 3.7
36	20-MAR-2017	Blood potassium	5.3 mmol/l	5.0 3.7
37	04-APR-2017	Blood potassium	5.4 mmol/l	5.0 3.7
38	10-JUN-2016	Blood urea	110 mg/dl	46 15
39	19-JUL-2016	Blood urea	45 mg/dl	46 15
40	16-AUG-2016	Blood urea	69 mg/dl	46 15
41	21-NOV-2016	Blood urea	75 mg/dl	46 15
42	14-FEB-2017	Blood urea	101 mg/dl	46 15
43	20-MAR-2017	Blood urea	92 mg/dl	46 15
44	04-APR-2017	Blood urea	102 mg/dl	46 15
45	19-JUL-2016	C-reactive protein	2.54 mg/dl	0.80 0.00
46	16-AUG-2016	C-reactive protein	1.17 mg/dl	0.80 0.00
47	21-NOV-2016	C-reactive protein	3.78 mg/dl	0.80 0.00
48	14-FEB-2017	C-reactive protein	0.32 mg/dl	0.80 0.00
49	20-MAR-2017	C-reactive protein	1.22 mg/dl	0.80 0.00
50	04-APR-2017	C-reactive protein	0.12 mg/dl	0.80 0.00
51	29-NOV-2016	Computerised tomogram	pulmonary embolism	
52	29-NOV-2016	Computerised tomogram	brain volume decreased	
53	16-NOV-2016	Echocardiogram	Middle up to high graded biatrialc dilatation	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
54	10-JUN-2016	Haematocrit	36 %	52 42
55	19-JUL-2016	Haematocrit	26.2 %	52 42
56	16-AUG-2016	Haematocrit	30.5 %	52 42
57	21-NOV-2016	Haematocrit	36.7 %	52 42
58	14-FEB-2017	Haematocrit	30.7 %	52 42
59	20-MAR-2017	Haematocrit	37.7 %	52 42
60	04-APR-2017	Haematocrit	39.4 %	52 42
61	10-JUN-2016	Haemoglobin	10.3 g/dl	18 14
62	19-JUL-2016	Haemoglobin	7.6 g/dl	18 14
63	16-AUG-2016	Haemoglobin	9.6 g/dl	18 14
64	16-AUG-2016	Haemoglobin	8.6 g/dl	18 14
65	21-NOV-2016	Haemoglobin	9.6 g/dl	18 14
66	14-FEB-2017	Haemoglobin	8.5 g/dl	18 14
67	20-MAR-2017	Haemoglobin	10.4 g/dl	18 14
68	04-APR-2017	Haemoglobin	10.9 g/dl	18 14
69	18-NOV-2016	Microbiology test	no pathogen, yeasts detected	
70	18-NOV-2016	Paracentesis	5000 ml	
71	10-JUN-2016	Platelet count	846 x10 3/mm3	
72	19-JUL-2016	Platelet count	428 x10 3/mm3	
73	16-AUG-2016	Platelet count	465 x10 3/mm3	
74	21-NOV-2016	Platelet count	647 x10 3/mm3	
75	14-FEB-2017	Platelet count	566 x10 3/mm3	
76	20-MAR-2017	Platelet count	521 x10 3/mm3	
77	04-APR-2017	Platelet count	442 x10 3/mm3	
78	19-JUL-2016	Protein total decreased	5.7 g/dl	8.0 6.5
79	10-JUN-2016	Red blood cell count	4.34 x10 6/mm3	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
80	19-JUL-2016	Red blood cell count	3.1 x10 6/mm3	
81	16-AUG-2016	Red blood cell count	3.36 x10 6/mm3	
82	21-NOV-2016	Red blood cell count	4.63 x10 6/mm3	
83	14-FEB-2017	Red blood cell count	3.88 x10 6/mm3	
84	20-MAR-2017	Red blood cell count	4.73 x10 6/mm3	
85	04-APR-2017	Red blood cell count	4.9 x10 6/mm3	
86	10-JUN-2016	White blood cell count	27.5 x10 3/mm3	
87	19-JUL-2016	White blood cell count	21.8 x10 3/mm3	
88	16-AUG-2016	White blood cell count	21.9 x10 3/mm3	
89	21-NOV-2016	White blood cell count	28.4 x10 3/mm3	
90	14-FEB-2017	White blood cell count	23.4 x10 3/mm3	
91	20-MAR-2017	White blood cell count	21.9 x10 3/mm3	
92	04-APR-2017	White blood cell count	19.8 x10 3/mm3	
93	14-NOV-2016	X-ray	right heart enlargement	
94	16-NOV-2016	X-ray	Increased showowing right lower field	
95	21-NOV-2016	X-ray	No change of basic findings	
96	24-NOV-2016	X-ray	No pneumothorax	
97	27-NOV-2016	X-ray	performed	
98	01-DEC-2016	X-ray	performed	
99	29-NOV-2016	X-ray limb	No evidence fracture	

13. Relevant Tests

PTH (10Jun2016): 91.8 pg/ml, (19Jul2016): 63.3, (16Aug2016): 112, (21Nov2016): 114, (14Feb2017): 73.6, (20Mar2017): 39.2, (04Apr2017): 59.1
Kt/V (dialysis effectivity/ dialysis dose x t/V; K = urea clearance due to dialysis in ml/min; t = duration of dialysis in min; V = urea distribution volume in ml) according to Daugirdas: 19Jul2016: 0.59, 16Aug2016: 1.27, 21Nov2016: 1.91, 14Feb2017: 2.28, 04Apr2017: 1.47 (units/range unspecified)
CXR (14Nov2016): when lying, right heart enlargement, right-sided effusion, also into interlobium, indication on potential infiltrations of lung, left lung seems free
Echo (16Nov2016): Middle up to high graded biatrialc dilatation, systolic function still given, paradox septum movements as indication of right heart complaint. Not determined: Ascites.
CXR (16Nov2016): increased shadowing in RLL, unsharp diaphragm crests both sides. State after extubation
CXR (21Nov2016): No change basic findings, enlarged shadow of heart, right sided pleural effusion
CT thorax (29Nov2016): Surrounded fresh thrombolic parts without complete obstruction in area of junction of segmentoid arteries

ADDITIONAL INFORMATION

13. Relevant Tests

and LLL. Perfusion in lower lobe in normal condition. Particularly Truncus pulmonalis and main pulmonary arteries free. Enlarged pleural effusion right sided with compression atelectasis in lower/middle lobes. No extensive pulmonary infiltrates. General cardiac expansion. Increasement of lymph nodes mediastal paraaortal. Liver/spleen enlargement with significant ascites in upper belly, GI tube/ central line left/right jugular
Skull CT (29Nov2016): brain volume decreased including bright inner/outer cerebrospinal fluid spaces, no indication circulation disorder, bleeding, dimension claim. No early signs of infarction. No edema, calcification of ACI in Siphon area. Inconspicuous areas of orbita. No injury of skull. Minor ventilation both mastoids and tympanon right. Circulary swellings of mucosa ethmoidal cells and sinus sphenoidalis

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	12000 IU, weekly 1st main dosage; Subcutaneous	Nephrogenic anemia (Nephrogenic anaemia)	16-AUG-2016 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		JUN	1930	86 Years	Male	87.50 kg	02	MAR	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

transient ischemic attack [Transient ischaemic attack]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a non-interventional study report from a contactable physician from the observational study, protocol EPOE-09-11, regarding subject 0930176.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
#2) MARCUMAR (PHENPROCOUMON)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, weekly	#1) Subcutaneous
#2) UNK	#2) Oral

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)
#2) atrial fibrillation (Atrial fibrillation)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 20-JAN-2016 / Ongoing	#1) Unknown
#2) Ongoing	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) PANTOZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Ongoing
#2) TORASEMID (TORASEMIDE) ; Ongoing
#3) RAMIPRIL (RAMIPRIL) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
06-JAN-2016 to Ongoing	Relevant Med History	Renal failure (Renal failure)
Unknown to Ongoing	Relevant Med History	Heart failure (Cardiac failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017103352

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-APR-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 86-uyear-old male Caucasian subject started epoetin zeta (RETACRIT) 4000 units subcutaneously per week on 20Jan2016 for the study indication of renal anemia. The first main dose was on 13Feb2017 at 4000 IU/week and the second dose was on 02Jan2017 at 8000 IU/week. The dose was changed within the last 3 months prior to the event on 11Jan2017 to 4000 IU. Hemoglobin prior to the dose change was 14.4 g/dl and afterwards was 13.0 g/dl. The subject never received any erythropoietin stimulating drugs. The subject was also taking phenprocoumon (MARCUMAR) by mouth for atrial fibrillation. The subject's medical history included renal failure since 06Jan2016, heart failure, hypertension, atrial fibrillation, and ischemic heart disease, all ongoing. His concomitant medications included pantoprazole sodium sesquihydrate (PANTOZOL) by mouth for prophylaxis, torasemide (TORASEMID) by mouth for prophylaxis, and ramipril by mouth for hypertension, all ongoing. The subject was hospitalized on 02Mar2017 for a transient ischemic attack (TIA). The onset date was reported as 02Mar2017. The subject was admitted with stroke symptoms. During his stay, a computerized tomogram (CT) of the head was done on 02Mar2017 that showed no signs of ischemia; therefore, a transient ischemic attack was diagnosed. The cause of the TIA was wrong dosage of anticoagulant phenprocoumon. Additional tests included PTH intact (normal range 0.015 - 0.065 ng/ml): 0.206 ng/ml on 21Nov2016, 0.240 ng/ml on 02Jan2017, 0.248 ng/ml on 13Feb2017, 0.244 ng/ml on 04Apr2017; potassium in serum (normal range 3.7-5.0 mmol/l): 3.7 mmol/l on 21Nov2016, 4.7 mmol/l on 02Jan2017, 5.4 mmol/l on 13Feb2017, 5.5 mmol/l on 03Apr2017; urea (normal range 15-46 mg/dl): 107 mg/dl on 21Nov2016, 112 mg/dl on 02Jan2017, 117 mg/dl on 13Feb2017, 92 mg/dl on 03Apr2017; CRP (sensitive) (normal range 0-0.80 mg/dl): 0.23 mg/dl on 21Nov2016, 2.37 mg/dl on 02Jan2017, 1.33 mg/dl on 13Feb2017, 1.32 mg/dl on 03Apr2017; hematocrit (normal range 42- 52 %): 45.5 % on 21Nov2016, 43 % on 02Jan2017, 40.6 % on 13Feb2017, 36.6 % on 03Apr2017; hemoglobin (normal range 14- 18 IU): 14.7 IU on 21Nov2016, 14.4 IU on 02Jan2017, 13.9 IU on 13Feb2017, 12.2 IU on 03Apr2017; thrombocytes: 144 x10 3/mm3 on 21Nov2016, 134 x10 3/mm3 on 02Jan2017, 146 x10 3/mm3 on 13Feb2017, 203 x10 3/mm3 on 03Apr2017; erythrocytes: 4.83 x10 3/mm3 on 21Nov2016, 4.73 x10 3/mm3 on 02Jan2017, 4.43 x10 3/mm3 on 13Feb2017, 3.86 x10 3/mm3 on 03Apr2017; leukocytes: 5.5 x10 3/mm3 on 21Nov2016, 7.1 x10 3/mm3 on 02Jan2017, 6.5 x10 3/mm3 on 13Feb2017, 3.86 x10 3/mm3 on 7.1 Apr2017 Hospital discharge report showed the subject was in inpatient treatment from 02Mar2017 to 08Mar2017. Diagnosis included left-hand side of the brain transitory ischemic attack in the service area of the A. cerebri media at ineffective "marcumarisation" (= medical treatment to reduce blood coagulation with coumarin-type drugs) at atrial fibrillation; initial sensomotoric aphasia and hemiparesis on the right ; here one-time bradyarrhythmia up to 48 S/min; arterial hypertension; dialysis-dependent kidney insufficiency; Condition after shaldon sepsis caused by E.coli; condition after herpes zoster infection; under therapy with Lyrica improvement of symptoms; unspecific increase of PSA as described above; and struma diffusa. Therapy: Current anamnesis and reason for inpatient admission: The inpatient neurological admission of the above mentioned subject occurred under the suspicion of a left sided ischemic at hemiparesis mainly concerning the arms on the right and global aphasia. The wife has noticed the above mentioned symptoms after getting up. A systemic lysis therapy did not come into consideration due to an unclear beginning of the symptoms and afterwards regressive symptoms. Subject administers MARCUMAR because of permanent atrial fibrillation. The coagulation parameters which have been determined at admission have been outside the therapeutic area (Quick 36%, INR 1.86). The subject has been around a year dialysis-dependent. The dialysis has been performed on Tuesday, Thursday and Saturday. Neurological findings at admission: No meningism, cervical spine freely moveable. No pain on percussion of the cranial vault. Sensomotoric aphasia with partial obtained speech intelligibility, dysarthria. The pupils are round on both sides, isocore sluggish reacting to light. Oculomotor system intact. Visual field at existing aphasia not adequate examinable. No nystagmus. No facial paresis. Hemiparesis mainly concerning the arms on the right, the short lifting of the arm was possible. Proprioceptive reflex sluggish everywhere. Babinski negative on both sides. Sensibility at aphasia only restrictively assessable, same reaction on pain stimuli on both sides. No rigor, no tremor, no hyper- or hypokinesia. Autonomic nervous system: bowl movement (subject has defecated). Psychopathologic findings at admission: At admission subject has been attentive and gave attention to the examiner. At sensomotoric aphasia an examination of the orientation is not possible. We see the subject as a psychomotor calm and cooperative person. Non-surgical findings at admission: The heart sounds have been clearly, arrhythmic and tachycardical auscultated. At the lungs there has been a vesicular breathing sound on both sides. The abdomen was soft, without any palpable resistances, with regular peristaltic. The subject has defecated. No outer signs of injuries, no tongue bite. Epicrisis: The inpatient neurological admission has been initiated by an emergency doctor. In the morning the wife has noticed a hemiparesis on the right as well as a communication disorder in terms of sensomotoric aphasia. The beginning of the symptoms has been unclear, hindermost the subject has been seen by his wife as normal at night, so that a systemic thrombolysis is not taken into consideration. The subject is anticoagulated with Marcumar because of his atrial fibrillation; the coagulation parameters at admission show an ineffective anticoagulation with Marcumar (Quick 36%, INR 1.86). A prompt visualization of the neurocranium through computer tomography has been performed, whereby no fresh territorial ischemic, no bleeding and no space-consuming lesion could be determined. The symptoms which lead to admission have already been regressive shortly after arriving into our hospital. The subject was admitted for further diagnostics into our stroke unit. Already on the next day the hemiparesis on the right was not detectable anymore, the aphasia has receded completely. A cranial computer tomography (CCT)-control supplemented during the course brought no modifications to the findings in comparison to the previous findings. We continued the oral anticoagulation with Marcumar and aimed for a final INR of 2,0 - 3,0. After consulting with the treating dialysis center an additional dialysis took place on Friday the 03Mar2017. During the inpatient stay the subject showed a bradyarrhythmia of 48 beats/minute, without detectable electrolyte imbalance or bradycardic medication. The subject showed to be symptom-free with this. We recommend an outpatient cardiologic introduction and a prompt echocardiography. The subject wished with no more symptoms to be discharged soon, so that an extensive cardiac diagnostic investigation was not possible for us to do. In an overall view on the findings a transitory ischemic attack in left- brain side supplying area of the Arteria cerebri media can be assumed with at time of admission existing, ineffective oral anticoagulation. The initial existing hemiparesis with emphasize on the right as well as the dysarthria and aphasia showed a quick and full regression. We adjusted the dosage of Marcumar and aimed at an final INR of 2,0 - 3,0. Because of a proven bradyarrhythmia we recommend further cardiological clarification within ambulatory care. On the 08Mar2017 we were able to discharge the subject without focal neurological findings from our inpatient neurological treatment. Computer tomography of the skull (02Mar2017): In comparison to the preliminary investigations within the practice from the

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

27Jun2016 questionable hyper-dense appearing arteria cerebri media bilateral, on the left-hand stressed, differential diagnosis vascular sclerosis/ stenosis, exsiccosis. No demarcated fresh ischemic infarct area. No bleedings. No signs of enhancing mass. No liquor circulation failure. At persistent clinic NMRI of the skull recommended for further diagnosis. Unaltered low micro angiopathic semioval center changes, bihemispheric, subcortical emphasized. Advanced involution signs with bi frontal emphasized expansion of the outer liquor rooms. Artheriosclerosis of the skull base near arteries. Osseous structures unobtrusive. Furthermore no changes to findings. Computer tomography of the skull from 07Mar2017: In comparison to the pre-examinations from 02Mar2017 no significant change of the findings could be shown. No hint at intracranial bleeding. No demarcate fresh ischemic territorial infarct areal. Unchanged about 8 mm large hypo-dense lesion subcortical on the right parieto-occipital in terms of an older cerebral infarct. Unchanged slight stained medullary layer changes on both sides periventricular and subcortical, most likely microangiopathic changes. Moderate involution signs at a bifrontal emphasized expanse of the exterior liquor spaces. Midsize, slightly expanded ventricular system. Known distinct vascular sclerosis in the area of the Arteria cerebri media on both sides. Remaining finding without change. Bony structures ordinary. Cardiologic council: Bradyarrhythmia up to 48 s/m without drugs against bradycardia and at known Atrial fibrillation. Picture of a right axis deviation with ventricular extrasystoles (VES), T-negative Augmented Voltage Left (AVL) Concerning the laboratory no electrolyte shift at dialysis-binding renal insufficiency. Duplex and Doppler sonography of the supra-aortal brain-supplying vessels: Aggravated and only restricted examination conditions at short neck. Slightly too moderately ubiquitous arteriosclerotic vasculopathy. As far as visible the arteria carotis communis (ACC), arteria carotis externa (ACE) and arteria carotis interna (ACI) have shown standard flow profile. Atrioventricular on both sides with orthograde flow, left > right presentable. Flat plaques in the bulb area without hemodynamic relevance. As far as assessable no hint at hemodynamic relevant stenosis or occlusion. TCD: Trans-temporal on both sides no sufficient acoustic window. Treatment recommendation: pantoprazol 20 mg 0-0-2, pregabalin (LYRICA) 25 mg 1-0-1, ramipril 10 mg 1-0-0 on dialysis free days, Furorese 500 mg 0,5-0-0 dialysis free days, marcumar according to value (target value INR 2.0-3.0), Dialysis: Tuesday, Thursday, Saturday. Out-subject cardiologic presentation recommended in case of bradyarrhythmia. No action was taken with epoetin zeta in response to the event. The action taken with phenprocoumon in response to the event was unknown; however, the medication was ongoing. On 08Mar2017, the subject was considered to have recovered from the event. It was reported that there was no causal relationship to epoetin zeta; however, a causal relationship was suspected to phenprocoumon because of a wrong dosage.

Follow-up (24Apr2017): New reported information received from the contactable physician includes: subject details, study drug details, medical history, tests, hospitalization dates, event details

Case Comment: The Company considered that there was a reasonable possibility that the event, transient ischemic attack, was related to treatment with epoetin zeta considering the known drug safety profile of an increased risk of thromboembolic events. Meanwhile, the subject's underlying multiple risk factors of transient ischemic attack including heart failure, hypertension, and atrial fibrillation can't be underestimated as well. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	21-NOV-2016	Blood parathyroid hormone increased	0.206 ng/ml	0.065 0.015
2	02-JAN-2017	Blood parathyroid hormone increased	0.240 ng/ml	0.065 0.015
3	13-FEB-2017	Blood parathyroid hormone increased	0.248 ng/ml	0.065 0.015
4	04-APR-2017	Blood parathyroid hormone increased	0.244 ng/ml	0.065 0.015
5	21-NOV-2016	Blood potassium	3.7 mmol/l	5.0 3.7
6	02-JAN-2017	Blood potassium	4.7 mmol/l	5.0 3.7
7	13-FEB-2017	Blood potassium	5.4 mmol/l	5.0 3.7
8	03-APR-2017	Blood potassium	5.5 mmol/l	5.0 3.7
9	21-NOV-2016	Blood urea	107 mg/dl	46 15
10	02-JAN-2017	Blood urea	112 mg/dl	46 15
11	13-FEB-2017	Blood urea	117 mg/dl	46

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				15
12	03-APR-2017	Blood urea	92 mg/dl	46 15
13	MAR-2017	Bradyarrhythmia	48 beats/minute	
14	21-NOV-2016	C-reactive protein increased	0.23 mg/dl	0.80 0
15	02-JAN-2017	C-reactive protein increased	2.37 mg/dl	0.80 0
16	13-FEB-2017	C-reactive protein increased	1.33 mg/dl	0.80 0
17	03-APR-2017	C-reactive protein increased	1.32 mg/dl	0.80 0
18	02-MAR-2017	Computerised tomogram	transient ischemic attack	
19	02-MAR-2017	Computerised tomogram	no fresh territorial ischemic, no bleeding	
20	03-MAR-2017	Computerised tomogram	no changes to previous findings	
21	07-MAR-2017	Computerised tomogram	no significant change of the findings	
22	21-NOV-2016	Haematocrit	45.5 %	52 42
23	02-JAN-2017	Haematocrit	43 %	52 42
24	13-FEB-2017	Haematocrit	40.6 %	52 42
25	03-APR-2017	Haematocrit	36.6 %	52 42
26	21-NOV-2016	Haemoglobin	14.7 IU	18 14
27	02-JAN-2017	Haemoglobin	14.4 IU	18 14
28	13-FEB-2017	Haemoglobin	13.9 IU	18 14
29	03-APR-2017	Haemoglobin	12.2 IU	18 14
30	02-MAR-2017	Heart sounds	clearly, arrhythmic and tachycard ausculatated	
31	02-MAR-2017	International normalised ratio	1.86	
32	02-MAR-2017	Neurological examination	Sensomotoric aphasia with partial obtained speech	
33	21-NOV-2016	Platelet disorder	144 x10 3/mm3	
34	02-JAN-2017	Platelet disorder	134 x10 3/mm3	
35	13-FEB-2017	Platelet disorder	146 x10 3/mm3	
36	03-APR-2017	Platelet disorder	203 x10 3/mm3	
37	02-MAR-2017	Prothrombin time	36 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
38	21-NOV-2016	Red blood cell scan	4.83 x10 6/mm3	
39	02-JAN-2017	Red blood cell scan	4.73 x10 6/mm3	
40	13-FEB-2017	Red blood cell scan	4.43 x10 6/mm3	
41	03-APR-2017	Red blood cell scan	3.86 x10 6/mm3	
42	MAR-2017	Ultrasound Doppler	Trans-temporal on both sides no sufficient acousti	
43	21-NOV-2016	White blood cell count	5.5 x10 3/mm3	
44	02-JAN-2017	White blood cell count	7.1 x10 3/mm3	
45	13-FEB-2017	White blood cell count	6.5 x10 3/mm3	
46	03-APR-2017	White blood cell count	7.1 x10 3/mm3	

13. Relevant Tests

computer tomography (02Mar2017): no fresh territorial ischemic, no bleeding and no space-consuming lesion could be determined. The symptoms which lead to admission have already been regressive shortly after arriving into our hospital. In comparison to the preliminary investigations within the practice from the 27Jun2016 questionable hyperdens appearing arteria cerebri media bilateral, on the left-hand stressed, differential diagnosis vascular sclerosis/ stenosis, exsiccosis. No demarcated fresh ischemic infarct area. No bleedings. No signs of enhancing mass. No liquor circulation failure. At persistent clinic NMRI of the skull recommended for further diagnosis. Unaltered low micro angiopathic semioval center changes, bihemispheric, subcortical emphasized. Advanced involution signs with bi frontal emphasized expansion of the outer liquor rooms. Artheriosklerosis of the skull base near arteries. Osseous structures unobtrusive. Furthermore no changes to findings.
Computer tomography of the skull (07Mar2017): In comparison to the pre-examinations from 02Mar2017 no significant change of the findings could be shown. No hint at intracranial bleeding. No demarcate fresh ischemic territorial infarct areal. Unchanged about 8 mm large hypodense lesion subcortical on the right parietooccipital in terms of an older cerebral infarct. Unchanged slight stained marklagerveranderung? on both sides periventricular and subcortical, most likely microangiopathic changes.
Moderate involution signs at a bifrontal emphasized expanse of the exterior liquor spaces. Midsize, slightly expanded ventricular system. Known distinct vascular sclerosis in the area of the Arteria cerebri media on both sides. Remaining finding without change. Bony structures ordinary.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	21	FEB	1933	84 Years	Female	67.00 kg	05	MAY	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
stroke [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study report from the observational study, protocol EPOE-09-11, regarding subject CR-005-0001.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, 2x/week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 23-SEP-2014 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN NOVO (INSULIN HUMAN) ; Unknown / 12-MAY-2017
#2) FURSEMID (FUROSEMIDE) ; Ongoing
#3) BYOL (BISOPROLOL FUMARATE) ; Ongoing
#4) ATORIS (ATORVASTATIN CALCIUM) ; Ongoing
#5) SYMBICORT (BUDESONIDE, FORMOTEROL FUMARATE) ; Ongoing
#6) ASKA (ACETYLSALICYLIC ACID) ; Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2014 to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease)
2012 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
	Fibrillatio atriorum intermitens	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017202601

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-MAY-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 84-year-old Caucasian female subject started epoetin zeta (RETACRIT) batch number (6Q019Q6), 2000 units subcutaneously two times a week, on 23Sep2014 for the study indication of renal anemia. The last dose prior to event was on 02May2017. The subject was previously receiving other ESA: eritropoetin beta (NEORECORMON) from an unknown date to 16Sep2014 at 30 IU/kg/week with hemoglobin at 118 g/l and didn't experience any thromboembolic event. Risk factors included obesity (BMI: 28.6 kg/m 2). The subject's medical history included coronary heart disease since 2014, atrial fibrillation since 2012, diabetes since 1995 and was on insulin therapy since 2002, hyperlipoproteinemia since 2014, hypertension since 2004, chronic obstructive lung disease (COPD) since 1998, chronic renal insufficiency, haemodialysis since Dec2013, osteoporosis, chronic lumbosacral syndrome, urinary incontinence, and non-smoker, all ongoing, stroke in 2002, heart failure in 2012, status post tuberculosis in 1996, status post fracture compressive vertebrate L2 and L4 in Sep2016. The following were the diagnosis: I63.5 CVI, G81.9 Hemiparesis lat. dex., I50.0 Cor atherosclerotic compensatum, J44.9 COPD, B90.9 St. post tbc pulmonum, N18.0 Insufficientia renalis chronica term., Z49.1 Hemodialysis iterative, I48 Fibrillatio atriorum intermitens, Interruptio conductionis, Insufficientia renalis chronica, E11.9 Diabetes mellitus type 2, E78.0 Dislipidemia, St. post fractura compressive verth. L2 et L4 (May2016), M60 Osteoporosis, M54 Sy. lumbosacrale chr., R32 Incontinetio urinae. Her concomitant medications included insulin human (INSULIN NOVO) 22 IU subcutaneously daily for diabetes from an unknown date to 12May2017, furosemide (FURSEMID) 80 mg once daily by mouth for heart failure, bisoprolol fumarate (BYOL) 1.25 mg once daily by mouth for atrial fibrillation, atorvastatin calcium (ATORIS) 10 mg once daily by mouth for hyperlipoproteinemia, budesonide/formoterol fumarate (SYMBICORT) 640/18 ug daily (frequenvy: 2x day) via respiratory inhalation for pulmonary disease, acetylsalicylic acid (ASKA) 100 mg once daily by mouth for atrial fibrillation, calcitriol (ROCALTROL) 0.25 ug once daily by mouth for renal bone disease, and calcium acetate/ magnesium carbonate (OSVAREN) 1.3 g/705 mg daily (frequency; 3x day) by mouth since 2014 for renal hyperphosphatemia, all ongoing. Type of dialysis: hemodialysis, mean dose 1 on 17Mar2017 was 30 IU/kg/week when hemoglobin was 116 g/l, mean dose 2 on 24Apr2017 was 60 IU/kg/week when hemoglobin was 97 g/l; there were dose changes within 3 months prior to event: The dose was changed on 24Apr2017, new dose was 60 IU/kg/week, hemoglobin prior to dose change: 97 g/l hemoglobin after dose change on 05May2017 was 118 g/l. The subject was hospitalized on 05May2017 for a life-threatening stroke, which was also reported to be medically significant and disabling. The onset date was reported as 05May2017. On this same date, a brain multi-slice computed tomography (MSCT) scan revealed acute ischemia/ ischemic lesion in left temporo-occipital region. Laboratory tests performed on 05May2017 included Activated partial thromboplastin time (APPT) 28.6 seconds, Activated partial thromboplastin time ratio (APPT R) 0.9, Creatinine 654, Fibrinogen 5.4 g/l, Glucose 10.2 mmol/l, C-reactive protein (CRP) 5.7, Glycosylated haemoglobin (HbA1c) 5.6%, Haematocrit 0.364, International normalised ratio (INR) 1, Platelet count 254 x 10^9/l, Prothrombin time (PT) 0.95, and HbA1c (05May2017): 38 mmol/mol. Urine test (05May2017): color -light yellow, clarity: cloudy, specific gravity: 1.015 kg/l, pH: 7.5, Leukocyte esterase: 3, nitrites: negative, proteins: 1, glucose: 0, ketones: 0, urobilinogen: normal, bilirubin: 0, erythrocytes/haemoglobin: in traces, sediment: many leucocytes, 1-2 erythrocytes, 1-2 platelet epithelial cells. Urgent brain MSCT (05May2017): On a series of native sections, infratentorial central and normally wide 4. ventricle is visible. Cerebellum and brain stem without any pathomorphological changes. Supratentorialy ventricle system is centrally located, symmetric, mild wider due to wider convexity sulci due to atrophic changes. No signs of hypertensive hydrocephalus. Along lateral brain ventricles, extensive chronic, hypoperfusion changes are visible. Basal cisterns are free. On the left, along the trigone of lateral ventricle, hyperdense branch of the blood vessel is visible, with smaller hypodense zone of cerebral parenchyma which corresponds to the hyperacute ischemic lesion. No signs of haemorrhage, expansive processes or extraaxial fluid collection are visible. Bones are intact. Heart and lung x-ray (05May2017): On the summation image of thoracic organs, the right hilum is more voluminous with decreased transparency of the perihilar lung parenchyma. Acute stagnation changes and pleural effusion weren't found. Doppler of carotid and vertebral arteries (08May2017): Color Doppler of carotids showed normal lumen width of both ACC and ACI arteries, with thickened walls with hard plaques at the bifurcation and proximal segments of ACI which on the left don't significantly protrude in lumen and don't cause morphological or hemodynamic stenosis or localized occlusive disease, while on the right side, in the proximal ACI segment they cause acceleration of blood flow due to haemodynamic stenosis for 60%. Bifurcation are located at the regular locations and are normally shaped. ACE have normal lumen width. Vertebral arteries are symmetrical, with normal lumen width and normal physiological route of blood circulation. Transcranial Doppler (08May2017): blood flow within the circle of Willis on the both sides is limited due to more ossified temporal parts. Vertebrobasilar circulation showed decreased mean velocity of blood flow in all examined blood vessels with physiological direction of circulation and regular resistivity index, which could indicate a VB insufficiency. Neurological exam (discharge letter summary) (12May2017): the patient was hospitalized due to acute, ischaemic cerebrovascular insult. On the brain MSCT on the left, along the trigone of lateral ventricle, hyperdense branch of the blood vessel is visible, with smaller hypodense zone of cerebral parenchyma which corresponds to the hyperacute ischemic lesion. Color Doppler of carotids without hemodynamic significant stenosis. She was examined by the internist. During hospitalization, she was in stable general condition, cardiorespiratory stable, afebrile. On the ward she was treated with antiaggregation therapy, low-molecular weight heparin, antihypertensive therapy, gastroprotective therapy, hypolipemic, infusions, and other symptomatic therapy. She received medical care and gymnastics. Her general condition improved with the therapy. At discharge, she could walk with someone else's help, she had normal verbal contact, severe right hemiparesis, urinary incontinence. She was discharged with stable general condition. Diagnosis at discharge: Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries. Treatment details were not provided. The subject was discharged on 12May2017. The subject recovered with sequelae on 12May2017. No action was taken with epoetin zeta in response to the event. It was reported that there was no causal relationship to epoetin zeta or concomitant medications.

Follow-up (18May2017): Updates subject's ethnicity, hospital discharge date, diagnosis information and event outcome.

Follow-up (23May2017): Updates study drug and concomitant product details, relevant history, past drug, laboratory test and other relevant tests including Brain MSCT, Doppler of carotid and vertebral arteries, Transcranial Doppler and Neurological exam summary.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event stroke was related to the study drug epoetin zeta. The event was most likely due to the subject's underlying cardiovascular conditions. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	05-MAY-2017	Activated partial thromboplastin time	28.6 seconds	
2	05-MAY-2017	Activated partial thromboplastin time ratio	0.9	
3	05-MAY-2017	Alanine aminotransferase	9 IU/l	
4	05-MAY-2017	Aspartate aminotransferase	19 IU/l	
5	05-MAY-2017	Blood chloride	96 mmol/l	
6	05-MAY-2017	Blood cholesterol	5.4 mmol/l	
7	05-MAY-2017	Blood creatine phosphokinase	33 IU/l	
8	05-MAY-2017	Blood creatinine	654 umol/l	
9	05-MAY-2017	Blood fibrinogen	5.4 g/l	
10	05-MAY-2017	Blood glucose	10.2 mmol/l	
11	05-MAY-2017	Blood lactate dehydrogenase	229 IU/l	
12	05-MAY-2017	Blood potassium	5.0 mmol/l	
13	05-MAY-2017	Blood sodium	139 mmol/l	
14	05-MAY-2017	Blood triglycerides	2.9 mmol	
15		Body mass index	28.6	
16	05-MAY-2017	C-reactive protein	5.7	
17	05-MAY-2017	Computerised tomogram head	acute ischemia	
18	05-MAY-2017	Gamma-glutamyltransferase	12 IU/l	
19	05-MAY-2017	Glycosylated haemoglobin	38	
20	05-MAY-2017	Glycosylated haemoglobin	5.6 %	
21	05-MAY-2017	Haematocrit	0.364	
22		Haemoglobin	118 g/l	
23	17-MAR-2017	Haemoglobin	116 g/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
24	24-APR-2017	Haemoglobin	97 g/l	
25	05-MAY-2017	Haemoglobin	118 g/l	
26	05-MAY-2017	High density lipoprotein	0.9 mmol/l	
27	05-MAY-2017	International normalised ratio	1	
28	05-MAY-2017	Low density lipoprotein	3.3 mmol/l	
29	05-MAY-2017	Mean cell haemoglobin	31.6 pg	
30	05-MAY-2017	Mean cell haemoglobin concentration	324 g/l	
31	05-MAY-2017	Mean cell volume	97.3	
32	05-MAY-2017	Mean platelet volume	10.0	
33	05-MAY-2017	Platelet count	254 x10 9/l	
34	05-MAY-2017	Prothrombin time	0.95	
35	05-MAY-2017	Red blood cell count	3.74 x10 12/l	
36	05-MAY-2017	Red cell distribution width	12.5 %	
37	05-MAY-2017	White blood cell count	9.2 x10 9/l	

13. Relevant Tests

HbA1c (05May2017): 38 mmol/mol
Urine test (05May2017): color -light yellow, clarity: cloudy, specific gravity: 1.015 kg/l, pH: 7.5, Leukocyte esterase: 3, nitrites: negative, proteins: 1, glucose: 0, ketones: 0, urobilinogen: normal, bilirubin: 0, erythrocytes/haemoglobin: in traces, sediment: many leucocytes, 1-2 erythrocytes, 1-2 platelet epithelial cells.
Urgent brain MSCT (05May2017): On a series of native sections, infratentorial central and normally wide 4. ventricle is visible. Cerebellum and brain stem without any pathomorphological changes. Supratentorialy ventricle system is centrally located, symmetric, mild wider due to wider convexity sulci due to atrophic changes. No signs of hypertensive hydrocephalus. Along lateral brain ventricles, extensive chronic, hypoperfusion changes are visible. Basal cisterns are free. On the left, along the trigone of lateral ventricle, hyperdense branch of the blood vessel is visible, with smaller hypodense zone of cerebral parenchyma which corresponds to the hyperacute ischemic lesion. No signs of haemorrhage, expansive processes or extraaxial fluid collection are visible. Bones are intact.
Heart and lung x-ray (05May2017): On the summation image of thoracic organs, the right hilum is more voluminous with decreased transparency of the perihilar lung parenchyma. Acute stagnation changes and pleural effusion weren't found.
Doppler of carotid and vertebral arteries (08May2017): Color Doppler of carotids showed normal lumen width of both ACC and ACI arteries, with thickened walls with hard plaques at the bifurcation and proximal segments of ACI which on the left don't significantly protrude in lumen and don't cause morphological or hemodynamic stenosis or localized occlusive disease, while on the right side, in the proximal ACI segment they cause acceleration of blood flow due to haemodynamic stenosis for 60%. Bifurcation are located at the regular locations and are normally shaped. ACE have normal lumen width. Vertebral arteries are symmetrical, with normal lumen width and normal physiological route of blood circulation.
Transcranial Doppler (08May2017): blood flow within the circle of Willis on the both sides is limited due to more ossified temporal parts. Vertebrobasilar circulation showed decreased mean velocity of blood flow in all examined blood vessels with physiological direction of circulation and regular resistivity index, which could indicate a VB insufficiency.
Neurological exam (discharge letter summary) (12May2017): the patient was hospitalized due to acute, ischaemic cerebrovascular insult. On the brain MSCT on the left, along the trigone of lateral ventricle, hyperdense branch of the blood vessel is visible, with smaller hypodense zone of cerebral parenchyma which corresponds to the hyperacute ischemic lesion. Color Doppler of carotids without hemodynamic significant stenosis. She was examined by the internist. During hospitalization, she was in stable general

ADDITIONAL INFORMATION

13. Relevant Tests

condition, cardiorespiratory stable, afebrile. On the ward she was treated with antiaggregation therapy, low-molecular weight heparin, antihypertensive therapy, gastroprotective therapy, hypolipemic, infusions, and other symptomatic therapy. She received medical care and gymnastics. Her general condition improved with the therapy. At discharge, she could walk with someone else's help, she had normal verbal contact, severe right hemiparesis, urinary incontinence. She was discharged with stable general condition. Diagnosis at discharge: Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) ROCALTROL (CALCITRIOL) ; Ongoing

#8) OSVAREN (CALCIUM ACETATE, MAGNESIUM CARBONATE) ; 2014 / Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2002 to 2002	Relevant Med History	Stroke (Cerebrovascular accident);
1995 to Ongoing	Relevant Med History diabetes mellitus type 2 on insulin therapy since 2002	Diabetes (Diabetes mellitus);
2014 to Ongoing	Relevant Med History	Hyperlipoproteinemia (Hyperlipidaemia);
2004 to Ongoing	Relevant Med History for the last 10 years	Hypertension (Hypertension);
2012 to Unknown	Relevant Med History	Heart failure (Cardiac failure);
1998 to Ongoing	Relevant Med History	Chronic obstructive lung disease (Chronic obstructive pulmonary disease);
1996 to Unknown	Relevant Med History St. post TBC pulmonum	Tuberculosis (Tuberculosis);
Unknown to Ongoing	Relevant Med History Insufficientia renalis chronica term.	Chronic renal insufficiency (Chronic kidney disease);
DEC-2013 to Ongoing	Relevant Med History Haemodialysis iterative 2x week	Haemodialysis (Haemodialysis);
SEP-2016 to Unknown	Relevant Med History	Fracture (Fracture);
Unknown to Ongoing	Relevant Med History	Osteoporosis (Osteoporosis);
Unknown to Ongoing	Relevant Med History	Lumbosacral syndrome (Cauda equina syndrome);
Unknown to Ongoing	Relevant Med History	Urinary incontinence (Urinary incontinence);
Unknown to 16-SEP-2014	Past Drug Event dose: 30 IU/kg/week Haemoglobin: 118 g/l	Neorecormon (NEORECORMON);
Unknown to Ongoing	Relevant Med History	Non-smoker (Non-tobacco user);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	17	NOV	1950	66 Years	Male	78.00 kg	03	MAY	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
thrombosis [Thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Pfizer-sponsored non-interventional study, protocol EPOE-09-11, regarding subject CR0120001.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) OCT-2015 / 03-APR-2017	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) RENVELA (SEVELAMER CARBONATE) ; 2016 / Ongoing
#2) ROCALTROL (CALCITRIOL) ; 2015 / Ongoing
#3) OSVAREN (CALCIUM ACETATE, MAGNESIUM CARBONATE) ; 2015 / Ongoing
#4) PANTOPRAZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 2014 / Ongoing
#5) SORBISTERIT-CALCIUM (CALCIUM POLYSTYRENE SULFONATE) ; 2015 / Ongoing
#6) CONCOR (BISOPROLOL FUMARATE) ; 2014 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1997 to Ongoing	Relevant Med History	Polycystic kidney (Congenital cystic kidney disease)
2004 to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017204715

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
31-MAY-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 66-year-old Caucasian male subject, described as not Hispanic or Latino, started epoetin zeta (RETACRIT, Solution for injection) 2000 IU subcutaneously weekly in Oct2015 for renal anemia. Product batch number: 6Q019Q6. There was a change in the dosage on 03Apr2017 from 2000 IU weekly to 2000 IU every other week. Hemoglobin prior to dose change was 11.8 g/dl and 11.0 g/dl after dose change. Mean dose 1 on 10Mar2017 was 2000 IU weekly when hemoglobin value was 11.9 g/dl; mean dose 2 on 03Apr2017 was 2000 IU every other week when hemoglobin value was 11.8 g/dl. Date of last dose prior to event: 24Apr2017. His medical history was significant for polycystic kidney disease since 1997, hypertension since 2004, terminal (end-stage) kidney disease (N18.0), infiltration in the middle lung lobe, polycystic liver disease, renal anemia, graft nephrectomy on 26Oct2015 due to dysfunction, left polycystic kidney nephrectomy on 19Oct2015, and graftectomy on 26Oct2015 due to inoperative transplanted kidney hydronephrosis, all ongoing, and kidney transplantation on 06Sep2015. The type of dialysis the subject was receiving was hemodialysis. The subject previously received other ESA: MIRCERA from 16Jan2015 to 06Sep2015 at 50 ug when hemoglobin value was 10.5 g/dl and didn't experience and thromboembolic event with any other ESA. The subject didn't have obesity (BMI: 24.9) nor did he have any other risk factors. Concomitant medications included sevelamer carbonate (RENVELA) 1600 mg 3 times daily since 2016 and calcium acetate/ magnesium carbonate (OSVAREN) 3 times daily since 2015, both for high blood phosphorus level; calcitriol (ROCALTROL) 0.5 ug once daily since 2015 for hyperparathyroidism, pantoprazole sodium sesquihydrate 20 mg once daily since 2014 for gastric protection, calcium polystyrene sulfonate (SORBISTERIT-CALCIUM) 20 g once daily since 2015 for hyperkalemia, bisoprolol fumarate (CONCOR) 1.25 mg once daily since 2014 for hypertension, and carbohydrates NOS/ fats NOS/ minerals NOS/ proteins NOS/ vitamins NOS (NEPRO HP) 220 ml once daily since 2014 for malnutrition. On 03May2017, the subject experienced thrombosis, considered serious for hospitalization and an important medical event. The vein thrombosis was associated with chronic hemodialysis vascular catheter in the subject's left internal jugular vein. After the AV fistula construction, swelling of the left hand was observed. Due to suspicion of stenosis due to the dialysis catheter, the catheter was removed. It was monitored since Apr2017. Due to progression of swelling of left hand, computerised tomogram (MSCT) was done on 03May2017, showing left brachiocephalic, left internal jugular, and proximal left subclavian vein thrombosis and partial thrombosis of the axillary vein. It was reported that the MSCT was done on 03May2017; the finding in writing was received 08May2017 when the physician arrived at work after the weekend. Treatment with low molecular weight heparin (LMWH) was initiated and "an overview of the intervention radiologist" was planned. The subject was admitted to the hospital due to the event on 15May2017. It was reported that the event was "threatening", but was not considered life threatening. Radiological intervention with stent placement in the left subclavian vein was performed. Percutaneous transluminal angioplasty was done on 17May2017. Venography was done on 17May2017 and it showed left brachiocephalic and subclavian vein thrombosis. The subject received heparin at 5000 IU intravenously and recanalization of the left subclavian vein and left brachiocephalic vein was done. Control venography showed mentioned veins with the normal flow. The radiologist recommended anticoagulant therapy 800 IU heparin/h/24 h in the infusion and oral anticoagulant therapy in the next 3 months. Anticoagulant therapy is anticipated for 3 months. No action was taken with epoetin zeta in response to the event. As of 19May2017, the subject was discharged from the hospitalization and was considered to be recovering from the event. The investigator reported that the event was unrelated to treatment with epoetin zeta or to any concomitant medications.

Follow-up (18May2017): Updates event seriousness, hospitalization date, study drug dosage regimen and start date, event outcome, concomitant medications, medical history, treatment.

Follow-up (31May2017): Updates concomitant medication details, event onset, subject status, action taken, hospitalization dates, treatment details

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported event thrombosis was related to the study drug but most likely related to the subject's chronic hemodialysis vascular catheter. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	06-FEB-2017	Activated partial thromboplastin time	24 seconds	28 22
2	09-MAY-2017	Activated partial thromboplastin time	23 seconds	28 22
3	06-MAR-2017	Alanine aminotransferase	24 IU/l	59 9
4	03-APR-2017	Alanine aminotransferase	IU/l	59 9
5	09-MAY-2017	Alanine aminotransferase	33 IU/l	59 9
6	09-MAY-2017	Alpha 1 globulin	1.8 g/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	09-MAY-2017	Alpha 1 globulin	2.9 %	3.2 1.9
8	09-MAY-2017	Alpha 2 globulin	10.2 %	12.6 7.9
9	09-MAY-2017	Alpha 2 globulin	6.4 g/l	
10	06-MAR-2017	Amylase	31 IU/l	91 23
11	06-MAR-2017	Aspartate aminotransferase	21 IU/l	34 11
12	09-MAY-2017	Aspartate aminotransferase	30 IU/l	34 11
13	06-FEB-2017	Basophil count	0.04 x10 9/l	0.06 0
14	06-MAR-2017	Basophil count	0.02 x10 9/l	0.06 0
15	03-APR-2017	Basophil count	0.02 x10 9/l	0.06 0
16	09-MAY-2017	Basophil count	0.03 x10 9/l	0.06 0
17	06-FEB-2017	Basophil percentage	0.7 %	1 0
18	06-MAR-2017	Basophil percentage	0.3 %	1 0
19	03-APR-2017	Basophil percentage	0.3 %	1 0
20	09-MAY-2017	Basophil percentage	0.6 %	1 0
21	09-MAY-2017	Beta globulin	10.0 %	12 7.5
22	09-MAY-2017	Beta globulin	6.3 g/l	
23	09-MAY-2017	Blood albumin	40.3 g/l	
24	09-MAY-2017	Blood albumin	64 %	70.5 59.2
25	06-MAR-2017	Blood alkaline phosphatase	97 IU/l	142 60
26	09-MAY-2017	Blood alkaline phosphatase	142 IU/l	142 60
27	09-MAY-2017	Blood bilirubin	15 umol/l	
28	06-FEB-2017	Blood calcium	2.07 mmol/l	2.53 2.14
29	06-MAR-2017	Blood calcium	2.07 mmol/l	2.53 2.14
30	03-APR-2017	Blood calcium	2.10 mmol/l	2.53 2.14
31	09-MAY-2017	Blood calcium	2.08 mmol/l	2.53 2.14
32	06-FEB-2017	Blood chloride	102 mmol/l	108 97

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33	03-APR-2017	Blood chloride	103 mmol/l	108 97
34	09-MAY-2017	Blood chloride	101 mmol/l	108 97
35	09-MAY-2017	Blood cholesterol	4.5 mmol/l	
36	06-MAR-2017	Blood creatine	841 umol/l	104 64
37	03-APR-2017	Blood creatine	823 umol/l	104 64
38	09-MAY-2017	Blood creatine	702 umol/l	104 64
39	06-FEB-2017	Blood fibrinogen	2.3 g/l	3.5 1.8
40	03-APR-2017	Blood fibrinogen	g/l	3.5 1.8
41	09-MAY-2017	Blood fibrinogen	2.9 g/l	3.5 1.8
42	03-APR-2017	Blood glucose	6.8 mmol/l	6.4 4.4
43	09-MAY-2017	Blood glucose	10.7 mmol/l	6.4 4.4
44	06-FEB-2017	Blood iron	11 umol/l	32 11
45	03-APR-2017	Blood iron	7 umol/l	32 11
46	09-MAY-2017	Blood iron	10 umol/l	32 11
47	06-FEB-2017	Blood phosphorus	1.28 mmol/l	1.42 0.79
48	06-MAR-2017	Blood phosphorus	0.97 mmol/l	1.42 0.79
49	03-APR-2017	Blood phosphorus	1.51 mmol/l	1.42 0.79
50	03-APR-2017	Blood phosphorus	mmol/l	
51	09-MAY-2017	Blood phosphorus	1.82 mmol/l	
52	06-FEB-2017	Blood potassium	5.2 mmol/l	5.1 3.9
53	06-MAR-2017	Blood potassium	5 mmol/l	5.1 3.9
54	03-APR-2017	Blood potassium	5.1 mmol/l	5.1 3.9
55	09-MAY-2017	Blood potassium	5.3 mmol/l	5.1 3.9
56	06-FEB-2017	Blood sodium	135 mmol/l	146 137
57	03-APR-2017	Blood sodium	136 mmol/l	146 137
58	09-MAY-2017	Blood sodium	134 mmol/l	146 137

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
59	06-MAR-2017	Blood urea	18.7 mmol/l	8.3 2.8
60	03-APR-2017	Blood urea	24.7 mmol/l	8.3 2.8
61	09-MAY-2017	Blood urea	23.2 mmol/l	8.3 2.8
62	03-APR-2017	Blood uric acid	433 umol/l	403 182
63	09-MAY-2017	Blood uric acid	409 umol/l	403 182
64		Body mass index	24.9	
65	06-MAR-2017	C-reactive protein	2 mg/l	5
66	09-MAY-2017	C-reactive protein	1.7 mg/l	5
67	03-MAY-2017	Computerised tomogram	thrombosis	
68	06-FEB-2017	Eosinophil count	0.18 x10 9/l	0.43 0
69	06-MAR-2017	Eosinophil count	0.13 x10 9/l	0.43 0
70	03-APR-2017	Eosinophil count	0.11 x10 9/l	0.43 0
71	09-MAY-2017	Eosinophil count	0.12 x10 9/l	0.43 0
72	06-FEB-2017	Eosinophil percentage	3.2 %	7 0
73	06-MAR-2017	Eosinophil percentage	2.3 %	7 0
74	03-APR-2017	Eosinophil percentage	1.8 %	7 0
75	09-MAY-2017	Eosinophil percentage	2.3 %	7 0
76	06-FEB-2017	Erythroblast count	0/100 leucoctyes %	
77	06-FEB-2017	Erythroblast count	0 x10 9/l	
78	06-MAR-2017	Erythroblast count	0 x10 9/l	
79	06-MAR-2017	Erythroblast count	0/100 leucocytes %	
80	03-APR-2017	Erythroblast count	0 x10 9/l	
81	03-APR-2017	Erythroblast count	0/100 leucocytes %	
82	09-MAY-2017	Erythroblast count	0/100 leucocytes %	
83	09-MAY-2017	Erythroblast count	0.0 x10 9/l	
84	06-MAR-2017	Gamma-glutamyltransferase	38 IU/l	55 11

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
85	09-MAY-2017	Gamma-glutamyltransferase	51 IU/l	55 11
86	06-FEB-2017	Haematocrit	0.342	0.530 0.415
87	06-MAR-2017	Haematocrit	0.358	0.530 0.415
88	03-APR-2017	Haematocrit	0.357	0.530 0.415
89	09-MAY-2017	Haematocrit	0.333	0.530 0.415
90	06-FEB-2017	Haemoglobin	111 g/l	175 138
91	06-MAR-2017	Haemoglobin	115 g/l	175 138
92	10-MAR-2017	Haemoglobin	119 g/l	175 138
93	03-APR-2017	Haemoglobin	118 g/l	175 138
94	09-MAY-2017	Haemoglobin	110 g/l	175 138
95	09-MAY-2017	High density lipoprotein	1.01 mmol/l	
96	09-MAY-2017	Immunoglobulins	12.9 %	16.3 9.0
97	09-MAY-2017	Immunoglobulins	8.1 g/l	
98	06-FEB-2017	International normalised ratio	1	3.5 2
99	09-MAY-2017	International normalised ratio	1	3.5 2
100	06-FEB-2017	Iron binding capacity total	58 umol/l	72 49
101	03-APR-2017	Iron binding capacity total	57 umol/l	72 49
102	09-MAY-2017	Iron binding capacity total	57 umol/l	72 49
103	06-FEB-2017	Iron binding capacity unsaturated	47 umol/l	54 25
104	03-APR-2017	Iron binding capacity unsaturated	50 umol/l	54 25
105	09-MAY-2017	Iron binding capacity unsaturated	47 umol/l	54 25
106	09-MAY-2017	Low density lipoprotein	2.8 mmol/l	
107	06-FEB-2017	Lymphocyte count	1.20 x10 9/l	3.35 1.19
108	06-MAR-2017	Lymphocyte count	0.96 x10 9/l	3.35 1.19
109	03-APR-2017	Lymphocyte count	0.91 x10 9/l	3.35 1.19
110	09-MAY-2017	Lymphocyte count	0.89 x10 9/l	3.35 1.19

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
111	06-FEB-2017	Lymphocyte percentage	21.2 %	46 20
112	06-MAR-2017	Lymphocyte percentage	16.7 %	46 20
113	03-APR-2017	Lymphocyte percentage	15.2 %	46 20
114	09-MAY-2017	Lymphocyte percentage	16.8 %	46 20
115	06-FEB-2017	Mean cell haemoglobin	30.1 pg	33.9 27.4
116	06-MAR-2017	Mean cell haemoglobin	30.3 pg	33.9 27.4
117	03-APR-2017	Mean cell haemoglobin	29.9 pg	33.9 27.4
118	09-MAY-2017	Mean cell haemoglobin	28.9 pg	33.9 27.4
119	06-FEB-2017	Mean cell haemoglobin concentration	329 g/l	345 320
120	06-MAR-2017	Mean cell haemoglobin concentration	321 g/l	345 320
121	03-APR-2017	Mean cell haemoglobin concentration	331 g/l	345 320
122	09-MAY-2017	Mean cell haemoglobin concentration	330 g/l	345 320
123	06-FEB-2017	Mean cell volume	92.7	97.2 83
124	06-MAR-2017	Mean cell volume	94.5	97.2 83
125	03-APR-2017	Mean cell volume	90.6	97.2 83
126	09-MAY-2017	Mean cell volume	87.6	97.2 83
127	06-FEB-2017	Mean platelet volume	12.3	10.4 6.8
128	06-MAR-2017	Mean platelet volume	13.4	10.4 6.8
129	03-APR-2017	Mean platelet volume	12.5	10.4 6.8
130	09-MAY-2017	Mean platelet volume	11.3	10.4 6.8
131	06-FEB-2017	Monocyte count	0.53 x10 9/l	0.84 0.12
132	06-MAR-2017	Monocyte count	0.49 x10 9/l	0.84 0.12
133	03-APR-2017	Monocyte count	0.40 x10 9/l	0.84 0.12
134	09-MAY-2017	Monocyte count	0.54 x10 9/l	0.84 0.12
135	06-FEB-2017	Monocyte percentage	9.3 %	12

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				2
136	06-MAR-2017	Monocyte percentage	8.5 %	12 2
137	03-APR-2017	Monocyte percentage	6.7 %	12 2
138	09-MAY-2017	Monocyte percentage	10.2 %	12 2
139	06-FEB-2017	Neutrophil count	3.72 x10 9/l	6.49 2.06
140	06-MAR-2017	Neutrophil count	4.15 x10 9/l	6.49 2.06
141	03-APR-2017	Neutrophil count	4.56 x10 9/l	6.49 2.06
142	09-MAY-2017	Neutrophil count	3.71 x10 9/l	6.49 2.06
143	06-FEB-2017	Neutrophil percentage	65.6 %	72 44
144	06-MAR-2017	Neutrophil percentage	72.2 %	72 44
145	03-APR-2017	Neutrophil percentage	76 %	72 44
146	09-MAY-2017	Neutrophil percentage	70.1 %	72 44
147	06-FEB-2017	Platelet count	152 x10 9/l	424 158
148	06-MAR-2017	Platelet count	141 x10 9/l	424 158
149	03-APR-2017	Platelet count	118 x10 9/l	424 158
150	09-MAY-2017	Platelet count	142 x10 9/l	424 158
151	09-MAY-2017	Protein total	63.0 g/l	
152	06-FEB-2017	Prothrombin time	1.02	0.70
153	09-MAY-2017	Prothrombin time	0.99	0.70
154	06-FEB-2017	Red blood cell count	3.69 x10 12/l	5.72 4.34
155	06-MAR-2017	Red blood cell count	3.79 x10 12/l	5.72 4.34
156	03-APR-2017	Red blood cell count	3.94 x10 12/l	5.72 4.34
157	09-MAY-2017	Red blood cell count	3.80 x10 12/l	5.72 4.34
158	06-FEB-2017	Red cell distribution width	15.1 %	15 9
159	06-MAR-2017	Red cell distribution width	14.3 %	15 9
160	03-APR-2017	Red cell distribution width	14.7 %	15 9
161	09-MAY-2017	Red cell distribution width	14.8 %	15 9

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
162	06-FEB-2017	Reticulocyte count	48 x10 9/l	97 22
163	03-APR-2017	Reticulocyte count	22.5 x10 9/l	97 22
164	09-MAY-2017	Reticulocyte count	22.4 x10 9/l	97 22
165	06-FEB-2017	Reticulocyte percentage	13 %	21.6 5
166	03-APR-2017	Reticulocyte percentage	5.7 %	21.6 5
167	09-MAY-2017	Reticulocyte percentage	5.9 %	21.6 5
168	09-MAY-2017	Serum ferritin	472.2	
169	06-FEB-2017	White blood cell count	5.67 x10 9/l	9.7 3.4
170	06-MAR-2017	White blood cell count	5.75 x10 9/l	9.7 3.4
171	03-APR-2017	White blood cell count	6 x10 9/l	9.7 3.4
172	09-MAY-2017	White blood cell count	5.29 x10 9/l	9.7 3.4

13. Relevant Tests

Multislice CT scan (03May2017): left brachiocephalic, left internal jugular, and proximal left subclavian vein thrombosis and partial thrombosis of the axillary vein.
Reticulocytes maturation (09May2017): 5.1; LFR = 94.9 %, MFR = 5.1 %, HFR = 0.0 %
APPT ratio (09May2017): 0.9
LDL/HDL (09May2017): 2.8
TGC (09May2017): 1.55 mmol/l
Ferritin (09May2017): 472.2 ug/l
Albumin/globulin (09May2017): 1.78
Reticulocyte maturation index (06Feb2017): 8.2 (normal range: 1.5-17.5)
LFR reticulocytes (06Feb2017): 91.8 % (normal range: 84.6-98.0)
MFR reticulocytes (06Feb2017): 7.4 % (normal range: 1.5-14.4
HFR reticulocytes (06Feb2017): 0.8 % (normal range: 0-2.4)
APPT ratio (06Feb2017): 0.9 (normal range: 0.8-1.2)
Fe/TIBC (09May2017). 0.18 (normal range: 020-0.55)
Reticulocyte maturation index (03Apr2017): 10.4 (normal range: 1.5-17.5)
LFR reticulocytes (03Apr2017): 89.6 % (normal range: 84.6-98.0)
MFR reticulocytes (03Apr2017): 8.7% (normal range: 1.5-14.4
HFR reticulocytes (03Apr2017): 1.7 % (normal range: 0-2.4)
Fe/TIBC (03Apr2017): 012 (normal range: 020-0.55)
Venography (17May2017): left brachiocephalic and subclavian vein thrombosis.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	2000 IU, every other week; Subcutaneous	renal anemia (Nephrogenic anaemia)	03-APR-2017 / Ongoing; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) NEPRO HP (CARBOHYDRATES NOS, FATS NOS, MINERALS NOS, PROTEINS NOS, VITAMINS NOS) ; 2014 / Ongoing

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
06-SEP-2015 to Unknown	Relevant Med History	Kidney transplant (Renal transplant);
Unknown to Ongoing	Relevant Med History N18.0	Terminal renal insufficiency (End stage renal disease);
Unknown to Ongoing	Relevant Med History	Lung infiltration (Lung infiltration);
Unknown to Ongoing	Relevant Med History	Polycystic liver disease (Polycystic liver disease);
Unknown to Ongoing	Relevant Med History	Renal anemia (Nephrogenic anaemia);
26-OCT-2015 to Ongoing	Relevant Med History	Nephrectomy (Nephrectomy);
19-OCT-2015 to Ongoing	Relevant Med History	Nephrectomy (Nephrectomy);
26-OCT-2015 to Ongoing	Relevant Med History	Nephrectomy (Nephrectomy); Graftectomy was done due to inoperative transplanted kidney hydronephrosis.
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);
16-JAN-2015 to 06-SEP-2015	Past Drug Event	Mircera (MIRCERA); dose: 50 mcg, haemoglobin: 10.5 g/dl

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1940	76 Years	Female	69.00 kg	15	MAR	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

thrombus of left coronary artery [Coronary artery thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a contactable physician from a Pfizer Sponsored non-interventional study, Protocol EPOE-09-11, regarding subject GE0930185.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 4000 IU, 3xweek

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 19-FEB-2016 / 15-MAR-2017

19. THERAPY DURATION
#1) 391 days

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Renal anaemia (Nephrogenic anaemia)
Unknown to Ongoing	Relevant Med History	Hypertension arterial (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017269786

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-MAR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 76-years-old female subject started to receive epoetin zeta (RETACRIT) 4000 IU subcutaneously three times a week on 19Feb2016 for renal anemia. On 22Feb2017 the dose of epoetin zeta was 12000 IU/week with hemoglobin at 11.8 g/dl, and on 19Dec2016 it was 12000 IU/week as well with hemoglobin at 13.1 g/dl. No changes in dose have been made in the 3 months prior to the event. The subject's medical history included renal anemia, arterial hypertension, and coronary triple vessel disease, all ongoing and hemodialysis. Concomitant medications were unknown. The subject was previously receiving another hemoglobin stimulating product, epoetin alfa (ABSEAMED) from 27Feb2012 to 17Feb2016 at 12000 IU/week with hemoglobin ranging from 8.9 -15.3 g/dl; the subject had no thromboembolic events under epoetin alfa. The subject was admitted to the hospital on 15Mar2017 with chest pain and dyspnea. A coronary catheter examination was conducted on 16Mar2017 which showed a thrombus of the left coronary artery, with an onset date of 15Mar2017. Following that, an in-stent DEB angioplasty was performed. The subject was discharged from the hospital on 18Mar2017 and was considered to have recovered from the event on the same date. The suspect product, epoetin zeta was discontinued on 15Mar2017, in response to the event. The investigator reported that there was no reasonable possibility that the event, thrombus of the left coronary artery, was related to the study drug or to any concomitant medications.

Follow-up (05Jul2017): Updates study drug information, medical history, past drug history, test data, action taken.

Amendment: This follow-up report is being submitted to amend previously reported information: to amend the patient's age at the event onset date and year of birth.

Case Comment: In agreement with the investigator, the Company considered that there was no reasonable possibility that the event, thrombus of the left coronary artery, was related to the study drug or to any concomitant medications. The underlying diseases of arterial hypertension and coronary heart disease provided more likely explanation to the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	29-NOV-2016	Blood creatinine	6.52 mg/dl	1.10 0.50
2	22-FEB-2017	Blood creatinine	5.81 mg/dl	1.10 0.50
3	10-APR-2017	Blood creatinine	6.03 mg/dl	1.10 0.50
4	29-NOV-2016	Blood parathyroid hormone	144 ng/ml	65 15
5	19-DEC-2016	Blood parathyroid hormone	167 ng/ml	65 15
6	22-FEB-2017	Blood parathyroid hormone	166 ng/ml	65 15
7	03-APR-2017	Blood parathyroid hormone	136 ng/ml	65 15
8	29-NOV-2016	Blood phosphorus	7.1 mg/dl	4.5 2.5
9	19-DEC-2016	Blood phosphorus	8.6 mg/dl	4.5 2.5
10	22-FEB-2017	Blood phosphorus	7.0 mg/dl	4.5 2.5
11	10-APR-2017	Blood phosphorus	8.8 mg/dl	4.5 2.5
12	29-NOV-2016	Blood potassium	4.0 mmol/l	5.0 3.7
13	19-DEC-2016	Blood potassium	3.7 mmol/l	5.0 3.7
14	22-FEB-2017	Blood potassium	6.0 mmol/l	5.0 3.7
15	10-APR-2017	Blood potassium	4.4 mmol/l	5.0 3.7
16	29-NOV-2016	C-reactive protein	0.83 mg/dl	0.80 0.00

Mfr. Control Number: 2017269786

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
17	19-DEC-2016	C-reactive protein	0.67 mg/dl	0.80 0.00
18	22-FEB-2017	C-reactive protein	1.02 mg/dl	0.80 0.00
19	10-APR-2017	C-reactive protein	0.7 mg/dl	0.80 0.00
20	16-MAR-2017	Catheterisation cardiac	thrombus of left coronary artery	
21	29-NOV-2016	Dialysis efficacy test	1.63	
22	19-DEC-2016	Dialysis efficacy test	1.62	
23	22-FEB-2017	Dialysis efficacy test	1.27	
24	29-NOV-2016	Haematocrit	38.8 %	47.0 37.0
25	19-DEC-2016	Haematocrit	38.8 %	47.0 37.0
26	22-FEB-2017	Haematocrit	37.8 %	47.0 37.0
27	10-APR-2017	Haematocrit	26.2 %	47.0 37.0
28	02-MAY-2017	Haematocrit	25.9 %	47.0 37.0
29		Haemoglobin	8.9-15.3 under Abseamed treatement g/dl	16.0 12.0
30	29-NOV-2016	Haemoglobin	13.2 g/dl	16.0 12.0
31	19-DEC-2016	Haemoglobin	13.1 g/dl	16.0 12.0
32	22-FEB-2017	Haemoglobin	11.8 g/dl	16.0 12.0
33	10-APR-2017	Haemoglobin	8.6 g/dl	16.0 12.0
34	02-MAY-2017	Haemoglobin	8.3 g/dl	16.0 12.0
35	29-NOV-2016	Platelet count	108 x10 3/mm3	400 150
36	22-FEB-2017	Platelet count	136 x10 3/mm3	400 150
37	10-APR-2017	Platelet count	118 x10 3/mm3	400 150
38	02-MAY-2017	Platelet count	144 x10 3/mm3	400 150
39	29-NOV-2016	Protein albumin ratio	6.7 g/dl	8.0 6.6
40	19-DEC-2016	Protein albumin ratio	6.6 g/dl	8.0 6.6
41	22-FEB-2017	Protein albumin ratio	6.4 g/dl	8.0 6.6
42	10-APR-2017	Protein albumin ratio	5.7 g/dl	8.0 6.6

Mfr. Control Number: 2017269786

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
43	29-NOV-2016	Red blood cell count	3.76 x10 6/mm3	5.40 4.20
44	19-DEC-2016	Red blood cell count	3.75 x10 6/mm3	5.40 4.20
45	22-FEB-2017	Red blood cell count	3.39 x10 6/mm3	5.40 4.20
46	02-MAY-2017	Red blood cell count	2.27 x10 6/mm3	5.40 4.20
47	29-NOV-2016	Serum ferritin	830 ng/ml	150 13
48	19-DEC-2016	Serum ferritin	791 ng/ml	150 13
49	22-FEB-2017	Serum ferritin	764 ng/ml	150 13
50	03-APR-2017	Serum ferritin	521 ng/ml	150 13
51	29-NOV-2016	White blood cell count	5.0 x10 3/mm3	10.0 4.3
52	19-DEC-2016	White blood cell count	5.7 x10 3/mm3	10.0 4.3
53	22-FEB-2017	White blood cell count	5.4 x10 3/mm3	10.0 4.3
54	10-APR-2017	White blood cell count	5.9 x10 3/mm3	10.0 4.3
55	02-MAY-2017	White blood cell count	8.3 x10 3/mm3	10.0 4.3

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Triple vessel disease (Coronary artery disease);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
27-FEB-2012 to 17-FEB-2016	Past Drug Event	Abseamed (ABSEAMED);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	17	APR	1936	81 Years	Male	63.00 kg	03	SEP	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombemboly legs [Peripheral embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II).

This is a report from a non-interventional clinical study, protocol EPO-09-11, regarding subject GE-432-0020.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 6000 IU, weekly	#1) Unknown

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 28-JUN-2017 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN INSUMAN (INSULIN HUMAN) ; 24-APR-2016 / Unknown
#2) PREDNISOLONE (PREDNISOLONE) ; 27-AUG-2014 / Unknown
#3) PANTOPRAZOLE (PANTOPRAZOLE) ; 27-AUG-2017 / Unknown
#4) BISOPROLOL (BISOPROLOL) ; 16-MAR-2015 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
10-FEB-2017 to Unknown	Relevant Med History	Rib fracture (Rib fracture)
NOV-2013 to Ongoing	Relevant Med History	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017389668

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 81-year-old Caucasian male subject received epoetin zeta subcutaneously 3 times weekly from 06Sep2016 to an unspecified date, 4000 IU weekend from 11May2017 to an unspecified date, then 6000 IU weekly since 28Jun2017 for the study indication of nephrogenic anemia. The most recent dose of the study drug prior to the event was administered on 31Aug2017. Two independent values of mean doses within 3 months prior to the event were reported as: 29Aug2017-6000 units/week; hemoglobin 10.0; and 11May2017-4000 units/week; hemoglobin 9.7. The subject's medical history included ongoing anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis since Nov2013, rib fracture on 10Feb2017, immobilization since 10Feb2017, diabetes mellitus, subdural hematoma with surgery on 05Jan2016, pneumonia in Jan2015, gastritis since 27Aug2014, hypertension since 16Mar2015 and dementia since 08Feb2017 ; the subject had not received any dialysis. He had not been exposed to any other erythropoietin-stimulating agents (ESAs). Concomitant medications included insulin human (INSULIN INSUMAN)18 IU twice daily (total daily 36 IU) from 24Apr2016 for diabetes, prednisolone 4 mg once daily from 27Aug2014 for vasculitis, pantoprazole 40 mg once daily from 27Aug2014 for gastritis, and bisoprolol 2.5 mg once daily from 16Mar2015 for hypertension. On an unspecified date, the subject developed sudden blue coloring of his legs within a short time; the right leg and upper left leg resolved within a short time, the left foot persisted for "this" days, then resolved spontaneously. The event was reported as thrombemboly legs, with the onset date of 03Sep2017, considered life-threatening and for which the subject was hospitalized on 03Sep2017. Peripheral arterial disease (PAD) since 04Sep2017 (date of diagnosis and considered risk factor for thromboembolic event). The subject was transferred from another hospital due to transient livid discoloration of both calves under preserved sensomotorics. A physical examination, date unspecified, showed reduced general state, lean nutritional state; left calf and foot cool, reddened, recapillarization 3-4 sec. On an unspecified date, color duplex sonography left showed three-phasic pelvis influx until APOP (not specified); arteria tibialis posterior suggestive three-phasic, arteria dorsalis pedis monophasic (60 cm/sec), perfunded. After evaluation a conservative approach was applied concerning calf arterial occlusive disease. After multiple queries the subject did not complain about pain at rest. In hospital, calves and feet were warm on both sides; recapillarization was delayed, sensomotorics were intact. No treatment was administered for the event. On 05Sep2017, the subject was discharged with stable calf arterial occlusive disease, considered recovered on that date. No action was taken with the study drug in response to the event. The investigator reported that there was a reasonable possibility that the event of thrombemboly legs was related to the study medication. On 17Nov2017, the investigator reported 'causality possible (as related to patient's medical history)'. The patient's pre-existing condition may well have triggered the condition but epoetin cannot be ruled out.

Follow-up (08Sep2017): Updates action taken, treatment data, medical history, risk factors, and concomitant medications.

Amendment: This follow-up report is being submitted to amend previously reported information: the correct dose of insulin human (INSULIN INSUMAN) was "Total daily dose" as "36 IU" with frequency reported as twice daily from 24Apr2016.

Follow-up (25Sep2017): Updates medical history, confirms date of diagnosis for PAD and action taken.

Follow-up (17Nov2017): Adds causality comment.

Follow-up (25Nov2017): New information received from the investigator includes answer to query: confirmed causality assessment.

Case Comment: In agreement with the investigator and considering the known safety profile, the Company considers there is a reasonable possibility that the reported thrombemboly legs is related to the use of epoetin zeta. However, underlying diabetes mellitus and vasculitis were significant risk factors in causing the event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	04-SEP-2017	Blood creatinine	5.4 mg/dl	1.2 0.7
2	04-SEP-2017	Blood glucose	164 mg/dl	100 60
3	04-SEP-2017	Blood phosphorus	5.2 mg/dl	4.5 2.5
4	04-SEP-2017	Blood urea	213 mg/dl	50 10
5	04-SEP-2017	Blood uric acid	8.7 mg/dl	7.0 3.4
6	04-SEP-2017	C-reactive protein	4.93 mg/dl	0.6 0.1
7	04-SEP-2017	Glomerular filtration rate	11 ml/min	60
8	04-SEP-2017	Glomerular filtration rate	9 ml/min	60

Mfr. Control Number: 2017389668

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
9	04-SEP-2017	Haematocrit	27.5 %	51,8 39,6
10		Haemoglobin	10 g/dl	17,7 13,9
11		Haemoglobin	9.7 g/dl	17,7 13,9
12	04-SEP-2017	Haemoglobin	9.1 g/dl	17,7 13,9
13	04-SEP-2017	Red blood cell count	3.12 x10 12/l	5.98 4.57
14	04-SEP-2017	Red cell distribution width	16.0 %	14,7 11,5
15	04-SEP-2017	Ultrasound Doppler	Color duplex sonography left: threephasic pelvis i	

13. Relevant Tests

Color duplex sonography (Date unknown): Left; threephasic pelvis influx until APOP (not specified); arteria tibialis posterior suggestive threephasic, arteria dorsalis pedis monophasic (60 cm/sec), perfunded.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	3x week; Subcutaneous	renal anemia (Nephrogenic anaemia)	06-SEP-2016 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	4000 IU, weekly; Unknown	renal anemia (Nephrogenic anaemia)	11-MAY-2017 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
NOV-2013 to Ongoing	Relevant Med History	Anti-neutrophil cytoplasmic antibody positive vasculitis (Anti-neutrophil cytoplasmic antibody positive vasculitis);
10-FEB-2017 to Unknown	Relevant Med History	Immobilization prolonged (Immobilisation prolonged);
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
05-JAN-2016 to Unknown	Relevant Med History	Subdural hematoma evacuation (Subdural haematoma evacuation);
JAN-2015 to JAN-2015	Relevant Med History	Pneumonia (Pneumonia);
27-AUG-2014 to Unknown	Relevant Med History	Gastritis (Gastritis);
16-MAR-2015 to Unknown	Relevant Med History	Hypertension (Hypertension);
08-FEB-2017 to Unknown	Relevant Med History	Dementia (Dementia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1960	57 Years	Female	Unk	05	SEP	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-interventional study, for protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 01-AUG-2016 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SANDIMMUN (CICLOSPORIN) ; 11-JAN-2010 / Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension arterial (Hypertension)
Unknown	Relevant Med History	Hypertensive heart disease (Hypertensive heart disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017437944

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-JUN-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 57-year-old female subject started to receive epoetin zeta (RETACRIT) 2000 IU subcutaneously twice weekly on 01Aug2016 for the study indication of nephrogenic anemia. The dose of epoetin zeta had not been changed within the three months prior to the event. The subject did not receive (pre) dialysis and had never before received erythropoietin-stimulating products. The subject's medical history included arterial hypertension, hypertensive heart disease, kidney graft, tertiary hyperparathyroidism and glomerulosclerosis from 2004 and ongoing. Concomitant medication included cyclosporin (SANDIMMUN) 75 mg twice daily since 11Jan2010 and ongoing for kidney transplant. On 05Sep2017, the subject suffered a myocardial infarction at home, received cardiopulmonary resuscitation (CPR) and was hospitalized. On 05Sep2017, ALT 43.5 IU/l, glucose 192.5 mg/l, triglycerides 114 mg/dl (high level 150), gamma-glutamyltransferase (GGT) 19.1 IU/l (range 0 - 55) and Troponin I 0.1388 ng/ml (range 0 - 0.0156). Her blood pressure was 140/73 mmHg, and thyroid stimulating hormone (TSH) 1.58 (range 0.35 - 4.94). Coronary angiography on 05Sep2017 revealed main stem: moderate coronary sclerosis, R. interventricularis anterior (RIVA) (left anterior descending: LAD): moderate coronary sclerosis; 80% stenosis of proximal RIVA near the ostium; occlusion of proximal RIVA. Right circumflex (RCX): moderate coronary sclerosis; right coronary artery (RCA): mild coronary sclerosis. Her diagnosis included atrial fibrillation in the presence of acute anterior wall non-ST segment myocardial infarction (NSTEMI); percutaneous coronary intervention (PCI) of 80% stenosis of the proximal RIVA near the ostium with drug-eluting stent (DES) placement (BiomatrixneoFlex), diameter achieved 3.9 mm; proximal RIVA occlusion with recanalization and placement of DES, diameter achieved 2.8 mm; atrioventricular (AV) block III degree with asystoles - placement of permanent pacemaker (Medtronic ENSURA DR MRI); arterial hypertension with hypertensive heart disease; status post kidney transplantation. On 06Sep2017, she underwent replacement/positioning of the pacemaker with good sensing, stimulus threshold LT 0.5. Additional conservative treatment included 12 months of combination therapy with acetylsalicylic acid (ASS) and ticagrelor. On 07Sep2017, ALT 24.3 IU/l, urea 87.7 mg/dl, CRP 75.55 mg/l and GGT 17.1 IU/l. Echocardiography on 07Sep2017 showed moderate concentric left-ventricular hypertrophy, good left ventricular pump function at rest. Wall movements: Discrete apical hypokinesis. Mitral valve with degenerative changes - most likely only mild mitral valve insufficiency, no mitral valve stenosis; degenerative changes of aortic valve - assessment: most likely only mild aortic valve insufficiency, mild to moderate aortic sclerosis. Assessment: left atrium slightly dilated. On 08Sep2017, ALT 14.1 IU/l, triglycerides 130 mg/dl, urea 71.1 mg/dl, and CRP 88.45. On 09Sep2017, ALT 9.1 IU/l, lactate dehydrogenase (LDH) 294 (high range 220), urea 87.3 mg/dl, and CRP 77.24 mg/l. On 10Sep2017, ALT 37.4 IU/l, LDH 287, urea 81.9 mg/dl, CRP 43.79 mg/l and GGT 5.3 IU/l. On 12Sep2017, CRP 31.93 mg/l. On 11Oct2017, ALT 9.2 IU/l, AST 2.32 IU/l, and CRP 2.32 mg/l. Pacemaker follow-up showed no re-programming was necessary; since reverse mode switch functions well without syncope and minimal need for RV stimulation, this mode is retained despite indication of AV block. Regarding kidney function: no acute need for action from a nephrological point of view, immunosuppression continued at cyclosporine (SANDIMMUNE) 75-0-75, mycophenolate mofetil (MMF) 1000 1-0-1, prednisone (DECORTIN) 5 mg; monitoring of parathyroid in the presence of tertiary hyperparathyroidism. No action was taken with the study drug in response to the event. The subject was discharged and considered recovered on 17Sep2017. The investigator reported there was no reasonable possibility that the event, myocardial infarction, was related to the study drug.

Follow-up (12Oct2017): Updates history, tests, study drug and event details, hospitalization dates, and treatment.

Follow-up (17Nov2017): Updates subject's age at event onset and suspect drug unit, confirms event term, adds investigator initial aware date and concomitant medication.

Follow-up (27Mar2018): New information reported from the site includes: correction of Subject ID.

Follow-up (18Jun2019): New information received from the investigator included: subject's birth year.

Case Comment: Based on the current available information, the company considered that there was not a reasonable possibility that the reported event myocardial infarction was related to subject drug of epoetin zeta. The event was most likely due to underlying medical conditions. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	16-JAN-2017	Alanine aminotransferase	5.9 IU/l	55 0
2	24-APR-2017	Alanine aminotransferase	8.8 IU/l	55 0
3	31-JUL-2017	Alanine aminotransferase	9.6 IU/l	55 0
4	05-SEP-2017	Alanine aminotransferase	43.5 IU/l	55 0
5	06-SEP-2017	Alanine aminotransferase	34.8 IU/l	55 0
6	07-SEP-2017	Alanine aminotransferase	24.3 IU/l	55 0

Mfr. Control Number: 2017437944

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	08-SEP-2017	Alanine aminotransferase	14.1 IU/l	55 0
8	09-SEP-2017	Alanine aminotransferase	9.1 IU/l	55 0
9	10-SEP-2017	Alanine aminotransferase	37.4 IU/l	55 0
10	11-OCT-2017	Alanine aminotransferase	9.2 IU/l	55 0
11	05-SEP-2017	Angiocardiogram	moderate coronary sclerosis main stem	
12	16-JAN-2017	Aspartate aminotransferase	1.46 IU/l	50 10
13	24-APR-2017	Aspartate aminotransferase	2.62 IU/l	50 10
14	31-JUL-2017	Aspartate aminotransferase	2.16 IU/l	50 10
15	11-OCT-2017	Aspartate aminotransferase	2.32 IU/l	50 10
16	05-SEP-2017	Blood glucose	192.5 mg/dl	105 70
17	09-SEP-2017	Blood lactate dehydrogenase	294	220
18	10-SEP-2017	Blood lactate dehydrogenase	287	220
19	SEP-2017	Blood pressure measurement	140/73 mmHg	
20	SEP-2017	Blood thyroid stimulating hormone	1.58	4.94 0.35
21	05-SEP-2017	Blood triglycerides	114 mg/dl	150
22	06-SEP-2017	Blood triglycerides	171 mg/dl	150
23	08-SEP-2017	Blood triglycerides	130 mg/dl	150
24	06-SEP-2017	Blood urea	97.2 mg/dl	43 21
25	07-SEP-2017	Blood urea	87.7 mg/dl	43 21
26	08-SEP-2017	Blood urea	71.1 mg/dl	43 21
27	09-SEP-2017	Blood urea	87.3 mg/dl	43 21
28	10-SEP-2017	Blood urea	81.9 mg/dl	43 21
29	16-JAN-2017	C-reactive protein	1.46 mg/l	5
30	24-APR-2017	C-reactive protein	2.62 mg/l	5
31	31-JUL-2017	C-reactive protein	2.16 mg/l	5
32	07-SEP-2017	C-reactive protein	75.55 mg/l	5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33	08-SEP-2017	C-reactive protein	88.45 mg/l	5
34	09-SEP-2017	C-reactive protein	77.24 mg/l	5
35	10-SEP-2017	C-reactive protein	43.79 mg/l	5
36	12-SEP-2017	C-reactive protein	31.93 mg/l	5
37	11-OCT-2017	C-reactive protein	2.32 mg/l	5
38	07-SEP-2017	Echocardiogram	LV hypertrophy	
39	05-SEP-2017	Gamma-glutamyltransferase	19.1 IU/l	55 0
40	06-SEP-2017	Gamma-glutamyltransferase	17.0 IU/l	55 0
41	07-SEP-2017	Gamma-glutamyltransferase	17.1 IU/l	55 0
42	10-SEP-2017	Gamma-glutamyltransferase	5.3 IU/l	55 0
43	05-SEP-2017	Troponin I	0.1388 ng/ml	0.0156 0

13. Relevant Tests

Coronary angiography (05Sep2017): main stem: moderate coronary sclerosis, R. interventricularis anterior (RIVA) (left anterior descending: LAD): moderate coronary sclerosis; 80% stenosis of proximal RIVA near the ostium; occulsion of proximal RIVA. Right circumflex (RCX): moderate coronary sclerosis; right coronary artery (RCA): mild coronary slcerosis.
Echocardiography (07Sep2017): Moderate concentric left-ventricular hypertrophy, good left ventricular pump function at rest. Wall movements: Discrete apical hypokinesis. Mitral valve with degenerative changes - most likely only mild mitral valve insufficiency, no mitral valve stenosis; degenerative changes of aortic valve - assessment: most likely only mild aortic valve insufficiency, mild to moderate aortic sclerosis. Assessment: left atrium slightly dilated.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2010 to Unknown	Relevant Med History	Kidney transplant (Renal transplant);
Unknown	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism);
2004 to Ongoing	Relevant Med History	Glomerulosclerosis (Glomerulosclerosis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	04	AUG	1967	49 Years	Male	92.00 kg	27	JUL	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
MI [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11, regarding subject SW005-0051.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 8000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 07-OCT-2015 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SODIUM BICARBONATE (SODIUM BICARBONATE) Tablet ; 16-OCT-2014 / Ongoing
#2) LOPERAMID MYLAN (LOPERAMIDE HYDROCHLORIDE) Capsule, ha
#3) ETALPHA (ALFACALCIDOL) Capsule, soft ; 18-JUN-2008 / Ongoing
#4) BEVIPLEX FORTE (NICOTINAMIDE, PYRIDOXINE HYDROCHLOR
#5) KALCIDON (CALCIUM CARBONATE) Chewable tablet ; 05-FEB-2014 / Ongoing
#6) INNOHEP (TINZAPARIN SODIUM) Solution for injection in pre-fil

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1987 to Ongoing	Relevant Med History	SLE (Systemic lupus erythematosus)
1997 to Ongoing	Relevant Med History	SLE nephritis (Lupus nephritis)
	dialysis	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017448837

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
08-NOV-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 49-year-old Caucasian male subject started to receive epoetin zeta (RETACRIT) 8000 IU twice a week subcutaneously on 07Oct2015 for the study indication of nephrogenic anemia. Date of last dose prior to the event was on 24Jul2017. Mean dose 1 on 19Jun2017: 6000 U, hemoglobin 84 g/l. Mean dose 2 on 20Jul2017: 8000 U, hemoglobin 88 g/l. Dose changes within 3 months prior to the event on 21Jun2017, new dose 8000. Hemoglobin prior to dose change 84 g/l. Hemoglobin after dose change on 31Aug2017: 96 g/l. The patient was not at any time exposed to any other erythropoetin-stimulating agents. The subject's medical history included systemic lupus erythematosus (SLE) since 1987, SLE nephritis since 1997 for which he receives hemodialysis, hypertension, inflammatory bowel disease (IBD), ischemic heart disease since May2016, all ongoing, subclavian vein stenosis in 1996 for which he underwent stenting due to restenosis of V. Subclavia Sin (known since 1996), and angio+PTCA on 24Jul2017, Risk factors for thromboembolic events included recent surgery 24Jul2017-24Jul2017: Angio+PTCA (V. Subclavia Sin.). It was reported that previous MI onset was not known. Concomitantly, the subject was taking sodium bicarbonate 2 tablets three times daily since 16Oct2014, loperamide hydrochloride (LOPERAMID MYLAN) 2 hard capsules as needed up to 8 capsules daily since 13Nov2015, alfacalcidol (ETALPHA) soft capsules since 18Jun2008, nicotinamide/ pyridoxine hydrochloride/ riboflavin sodium phosphate/ thiamine hydrochloride (BEVIPLEX FORTE) 1 film-coated tablet once daily since 21Jun2017, calcium carbonate (KALCIDON) chewable tablet 150 mg three times daily since 05Feb2014 for high phosphate, tinzaparin socim (INNOHEP) solution for injection in pre-filled syringe 2500 IU at dialysis since 21Apr2016, iron dextran (COSMOFER) solution for injection/infusion 2 ml intravenously every other Monday at dialysis since 10Nov2015, cyanocobalamin (BEHEPAN) film-coated tablet 1 mg once daily since 11Jul2017 against B12 deficiency, doxazosin mesilate (ALFADIL) modified-release tablet 8 mg once daily since 23Dec2016, furosemide (FURIX) tablet 500 mg once daily since 31Oct2015, metoprolol succinate (METOPROLOL ORION) modified-release tablet 100 mg twice daily since 26Nov2015 for heart and blood pressure, prednisolone (PREDNISOLONE PFIZER) tablet 5 mg once daily since 22May2013, immunoglobulin human normal (GAMMANORM) solution for injection subcutaneously since 11Apr2016, allopurinol (ALLOPURINOL NORDIC DRUGS) tablet 100 mg once daily since 11Jan2013 against gout, sevelamer carbonate (SEVELAMER TEVA) film-coated tablet 1600 mg three times daily since 12Feb2017 against high phosphate, and paracetamol (ALVEDON) 2 modified-release tablets three times daily as needed since 15May2017 against pain, all ongoing. On 27Jul2017 the subject experienced a myocardial infarction (MI). The subject was not hospitalized due to the event, but was considered life-threatening and an important medical event. Tests on 27Jul2017 included electrocardiogram (ECG) QRS duration showed: 108 ms. ECG PQ-time: 182; High QRS+large P wave gives suspicion of left chamber hypertrophy? STT alterations. Anterior wall infarction; ECG QT/QTc: 342/434 ms. Anterior wall infarction; ECG PRT axis: 63, 12, 121. ECG Ventricular frequency: 97 B/M, Normal sinus rhythm. No ECG available for comparison. On 31Jul2017 ECG showed new alterations compared to previous ECG. T waves in leads II, aVF and III. Additionally, T waves in V2 and V3 have supervened. In V3, a supervened wave of unclear etiology is seen. The case was discussed with cardiology consult who assessed that they should continue with the investigation with echocardiography. Echocardiography on 31Jul2017 - evaluation: left chamber slightly dilated. Systolic function is slightly to moderately decreased, with regionality within apical segments. Light mitralis insufficiency, functional. Right side without remarks. Myocardial scintigraphy on 07Aug2017 evaluation: Myocardial scintigraphy with findings as at large myocardial lesion, apically- middle and lower part of anterior wall with anteroseptal distribution ('corresponding to at least v35% of VK myocard, LAD') and quite pronounced decreased global systolic function with EF 25-30%. No certain ischemia detected in connection to this area, but possibly a smaller element of ischemia exists in the inferior wall (corresponding to maxium 5-10% of VK myocard, RCA). On 07Aug2017 ECG at rest: Sinus rhythm 90/min. QRS amplitudes that give suspicion of left chamber hypertrophy. ST-T alterations. Pathological R-wave progression with Q wave in V3-V4. Ventricular frequency 90. Compared to 31Jul2017 essentially unchanged. Diagnostic tests result for cerebrovascular accident and pulmonary embolism not available. Additional tests included hemoglobin on 15Jun2017 was 83, on 20Jul2017 was 88 (Reference interval 134-170 g/L). Hematocrit on 15Jun2017 was 0.25, on 20Jul2017 was 0.28 (Reference interval 0.4-0.5). Erythrocytes on 15Jun2017 was 2.8, on 20Jul2017 was 3.0 (Reference interval 4.3-5.7 x10^12). Mean cell volume on 15Jun2017 was 92, on 20Jul2017 was 94 (Reference interval 82-98fL). Mean cell hemoglobin on 15Jun2017 was 30, on 20Jul2017 was 30 (Reference interval 27-33 pg). Mean cell hemoglobin concentration on 15Jun2017 was 328, on 20Jul2017 was 316 (Reference interval 320-360 g/l). White blood cell count on 15Jun2017 was 6.9, on 20Jul2017 was 8.4 (Reference interval 3.5-8.8 x10^9/L). Platelet count on 15Jun2017 was 263, on 20Jul2017 was 246 (Reference interval 140-350 x10^9/L). Blood bicarbonate on 15Jun2017 was 23.6 (Reference interval 19.0-26.0 mmol/L). Base excess standard on 15Jun2017 was 0.0 (Reference interval -3.0-3.0 mmol/L). Iron on 15Jun2017 was 6.3 (Reference interval 9-34 umol/L). Transferrin on 15Jun2017 was 1.12 (Reference interval 1.9-3.3 g/l). Transferrin saturation on 15Jun2017 was 0.22 (Reference interval 0.15-0.60, no units provided). P-Ferritin on 15Jun2017 was 831 (Reference interval 34-275 ug/L). P-Sodium on 15Jun2017 was 143, on 20Jul2017 was 142 (Reference interval 137-145 mmol/l). P-Potassium on 15Jun2017 was 3.4, on 20Jul2017 was 4.5 (Reference interval 3.5-4.4 mmol/l). P-Calcium on 15Jun2017 result 2.51 (Reference interval 2.15-2.50 mmol/l). P-phosphate on 15Jun2017 result 1.8 (Reference interval 0.7-1.6 mmol/l). P-Creatinine on 15Jun2017 was 1052, on 20Jul2017 was 854, both described as alarm value (Reference interval 60-105 umol/l). Pt-Crea, eGFR, MDRD on 15Jun2017 was 5, on 20Jul2017 was 13, absolute eGFR (Reference interval >60 ml/min/1.73^2). P-Urea on 15Jun2017 was 17.8 (Reference interval 3.2-8.1 mmol/l). P-Albumin on 15Jun2017 was 29 (Reference interval 36-45 g/l). P-ALP on 15Jun2017 was 1.1 (Reference value 0.60-1.8 ukat/l). P-AST on 15Jun2017 was 0.20 (Reference value <0.76 ukat/l). P-ALT on 15Jun2017 was 0.21 (Reference value <1.2 ukat/l). P-PTH on 15Jun2017 was 85 (Reference value 1.6-6.9 pmol/l). S-Calcium ion activity on 15Jun2017 was 1.32 (Reference value 1.15-1.33 mmol/l). Body weight on 20Jul2017 was 102.5 kg. P-APTT on 20Jul2017 was 25 (Reference interval 24-32 seconds). P-PK-INR on 20Jul2017 was 1.0 (Reference interval 0.8-1.2). No action was taken with epoetin zeta as a result of the event. It was reported that "CORAI" is planned. The subject was considered to have recovered with unspecified sequelae on an unspecified date. The investigator reported that there was not a reasonable possibility that the event MI was related to the study drug or to a concomitant drug.

Follow-up (02Nov2017): Updates seriousness criteria (life-threatening), medical history, study drug details, event outcome, tests

Mfr. Control Number: 2017448837

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Follow-up (08Nov2017): Updates tests.

Case Comment: In agreement with the investigator, Company considered that there was not a reasonable possibility that the event "myocardial infarction" was related to study drug or any concomitant medication, the event was most likely related to underlying medical conditions. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	20-JUL-2017	Activated partial thromboplastin time	25 seconds	32 24
2	15-JUN-2017	Alanine aminotransferase	0.21 ukat/l	1.2
3	15-JUN-2017	Aspartate aminotransferase	0.20 ukat/l	0.76
4	15-JUN-2017	Blood albumin	29 g/l	45 36
5	15-JUN-2017	Blood alkaline phosphatase	1.1 ukat/l	1.8 0.6
6	15-JUN-2017	Blood bicarbonate	23.6 mmol/l	26.0 19.0
7	15-JUN-2017	Blood calcium	2.51 mmol/l	2.5 2.15
8	15-JUN-2017	Blood creatinine	1052 umol/l	105 60
9	20-JUL-2017	Blood creatinine	854 umol/l	105 60
10	15-JUN-2017	Blood iron	6.3 umol/l	34 9
11	15-JUN-2017	Blood parathyroid hormone	85 pmol/l	6.9 1.6
12	15-JUN-2017	Blood phosphorus	1.8 mmol/l	1.6 0.7
13	15-JUN-2017	Blood potassium	3.4 mmol/l	4.4 3.5
14	20-JUL-2017	Blood potassium	4.5 mmol/l	4.4 3.5
15	15-JUN-2017	Blood sodium	143 mmol/l	145 137
16	20-JUL-2017	Blood sodium	142 mmol/l	145 137
17	15-JUN-2017	Blood urea	17.8 mmol/l	8.1 3.2
18	15-JUN-2017	Calcium ionised	1.32 mmol/l	1.33 1.15
19	31-JUL-2017	Echocardiogram	Left chamber sligthtly dilated	
20	27-JUL-2017	Electrocardiogram	Normal sinus rhythm	
21	31-JUL-2017	Electrocardiogram	new alterations compared to previous	
22	07-AUG-2017	Electrocardiogram	Compared to 31Jul2017 essentially unchanged.	
23	27-JUL-2017	Electrocardiogram PR interval	182	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
24	27-JUL-2017	Electrocardiogram QT interval	342	
25	27-JUL-2017	Electrocardiogram QT interval	434	
26	15-JUN-2017	Glomerular filtration rate	5 ml/min/1.73^2	60
27	20-JUL-2017	Glomerular filtration rate	13 ml/min/1.73^2	60
28	15-JUN-2017	Haematocrit	0.25	0.5 0.4
29	20-JUL-2017	Haematocrit	0.28	0.5 0.4
30	15-JUN-2017	Haemoglobin	83 g/l	170 134
31	19-JUN-2017	Haemoglobin	84 g/l	170 134
32	20-JUL-2017	Haemoglobin	88 g/l	170 134
33	31-AUG-2017	Haemoglobin	96 g/l	170 134
34	20-JUL-2017	International normalised ratio	1.0	1.2 0.8
35	15-JUN-2017	Mean cell haemoglobin	30 pg	33 27
36	20-JUL-2017	Mean cell haemoglobin	30 pg	33 27
37	15-JUN-2017	Mean cell haemoglobin concentration	328 g/l	360 320
38	20-JUL-2017	Mean cell haemoglobin concentration	316 g/l	360 320
39	15-JUN-2017	Mean cell volume	92 fL	98 82
40	20-JUL-2017	Mean cell volume	94 fL	98 82
41	15-JUN-2017	Platelet count	263 x10 9/l	350 140
42	20-JUL-2017	Platelet count	246 x10 9/l	350 140
43	27-JUL-2017	QRS axis	108	
44	15-JUN-2017	Red blood cell count decreased	2.8 x10 12/l	5.7 4.3
45	20-JUL-2017	Red blood cell count decreased	3.0 x10 12/l	5.7 4.3
46	07-AUG-2017	Scan myocardial perfusion	at large myocardial lesion	
47	15-JUN-2017	Serum ferritin	831 ug/l	275 34
48	27-JUL-2017	Sinus rhythm	97	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
49	07-AUG-2017	Sinus rhythm	90	
50	15-JUN-2017	Transferrin	1.12 g/l	3.3 1.9
51	15-JUN-2017	Transferrin saturation	0.22	0.6 0.15
52	20-JUL-2017	Weight	102.5 kg	
53	15-JUN-2017	White blood cell count	6.9 x10 9/l	8.8 3.5
54	20-JUL-2017	White blood cell count	8.4 x10 9/l	8.8 3.5

13. Relevant Tests

ECG Ventricular frequency (27Jul2017): 97 B/M, Normal sinus rhythm
ECG PQ-time (27Jul2017): 182 ms. High QRS+large P wave gives suspicion of left chamber hypertrophy? STT alterations. Anterior wall infarction.
ECG QRS duration (27Jul2017): 108 ms. High QRS+large P wave gives suspicion of left chamber hypertrophy? STT alterations. Anterior wall infarction.
ECG QT/QTc (27Jul2017): 342/434 ms. Anterior wall infarction.
ECG PRT axis (27Jul2017): 63, 12, 121. No ECG available for comparison.
ECG (31Jul2017): ECG taken today shows new alterations compared to previous ECG. T waves in leads II, aVF and III. Additionally, T waves in V2 and V3 have supervened. In V3, a supervened wave of unclear etiology is seen. The case was discussed with cardiology consult who assesses that we should continue with the investigation with Echocardiography.
Echocardiography (31Jul2017): Evaluation: Left chamber sligthtly dilated. Systolic function is sligthly to moderately decreased, with regionality within apical segments. Light mitralis insufficiency, functional. Right side without remarks.
Myocardial scintigraphy (07Aug2017): Evaluation: Myocardial scintigraphy with findings as at large myocardial lesion, apically- middle and lower part of anterior wall with anteroseptal distribution ('corresponding to at least v35% of VK myocard, LAD') and quite pronounced decreased global systolic function with EF 25-30%. No certain ischemia detected in connection to this area. but possibly a smaller element of ischemia exists in the inferior wall (corresponding to maxium 5-10% of VK myocard, RCA).
ECG at rest (07Aug2017): Sinus rhythm 90/min. QRS amplitudes that give suspicion of left chamber hypertrophy. ST-T alterations. Pathological R-wave progression with Q wave in V3-V4. Compared to 31Jul2017 essentially unchanged.
Base excess standard (15Jun2017) Reference interval -3,0-3,0 mmol/L, result: 0,0 mmol/L.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	6000 IU, UNK; Subcutaneous	nephrogenic anemia (Nephrogenic anaemia)	19-JUN-2017 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	8000 IU, UNK; Subcutaneous	nephrogenic anemia (Nephrogenic anaemia)	20-JUL-2017 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) LOPERAMID MYLAN (LOPERAMIDE HYDROCHLORIDE) Capsule, hard ; 13-NOV-2015 / Ongoing

#4) BEVIPLEX FORTE (NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN SODIUM PHOSPHATE, THIAMINE HYDROCHLORIDE) Film-coated tablet ; 21-JUN-2017 / Ongoing

#6) INNOHEP (TINZAPARIN SODIUM) Solution for injection in pre-filled syringe ; 21-APR-2016 / Ongoing

#7) COSMOFER (IRON DEXTRAN) Solution for injection/infusion ; 10-NOV-2015 / Ongoing

#8) BEHEPAN (CYANOCOBALAMIN) Film-coated tablet ; 11-JUL-2017 / Ongoing

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#9) ALFADIL (DOXAZOSIN MESILATE) Modified-release tablet ; 23-DEC-2016 / Ongoing

#10) FURIX (FUROSEMIDE) Tablet ; 31-OCT-2015 / Ongoing

#11) METOPROLOL ORION (METOPROLOL SUCCINATE) Modified-release tablet ; 26-NOV-2015 / Ongoing

#12) PREDNISOLONE PFIZER (PREDNISOLONE) Tablet ; 22-MAY-2013 / Ongoing

#13) GAMMANORM (IMMUNOGLOBULIN HUMAN NORMAL) Solution for injection ; 11-APR-2016 / Ongoing

#14) ALLOPURINOL NORDIC DRUGS (ALLOPURINOL) Tablet ; 11-JAN-2013 / Ongoing

#15) SEVELAMER TEVA (SEVELAMER CARBONATE) Film-coated tablet ; 12-FEB-2017 / Ongoing

#16) ALVEDON (PARACETAMOL) Modified-release tablet ; 15-MAY-2017 / Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1996 to Unknown	Relevant Med History stent	Subclavian vein stenosis (Subclavian vein stenosis);
Unknown	Relevant Med History	Stent placement (Stent placement);
24-JUL-2017 to 24-JUL-2017	Relevant Med History	Angioplasty (Angioplasty);
24-JUL-2017 to 24-JUL-2017	Relevant Med History	Percutaneous transluminal coronary angioplasty (Coronary angioplasty);
MAY-2016 to Ongoing	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	IBD (Inflammatory bowel disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	CROATIA	06	DEC	1939	77 Years	Female	62.50 kg	24	OCT	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

CVI [Cerebral infarction]
Diarrhoea [Diarrhoea]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, Protocol EPOE-09-11 (C1111006), regarding subject CR0090010.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 28-MAY-2014 / 08-JUN-2017	#1) 1108 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) EBRANTIL (URAPIDIL) ; Unknown
#2) TRIPLIXAM (AMLODIPINE BESILATE, INDAPAMIDE, PERINDOP
#3) CONTROLOC (PANTOPRAZOLE) ; Ongoing
#4) ATORIS (ATORVASTATIN CALCIUM) ; Ongoing
#5) ZEMPLAR (PARICALCITOL) ; Ongoing
#6) MOXONIDIN (MOXONIDINE) ; FEB-2017 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia) 10Jun2011-06Jul2011 acute MI hospitalization. ;30May2015-16Jun2015 acute NSTEMI hospitalization
2010 to Unknown	Relevant Med History	Transient ischemic attack (Transient ischaemic attack)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017468071

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-DEC-2017

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This 77-year-old Caucasian female subject started to receive epoetin zeta (RETACRIT) 4000 IU subcutaneously once weekly from 28May2014 to 08Jun2017 and then 6000 IU once weekly since 08Jun2017 for the study indication of renal anemia. The date of last dose prior to event was on 24Oct2017. On 12Sep2017, mean dose 1 was 96 IU/kg with hemoglobin 11.2 g/dl. On 14Oct2017, mean dose 2 was 96 IU/kg with hemoglobin 11.0 g/dl. There have not been any dose changes within 3 months prior to the event. The subject was not receiving any other erythropoietin stimulating agents. The subject's medical history was significant for hyperlipidemia, hypertension, hemodialysis 3 times weekly since 28Apr2017, atrial fibrillation since 16May2017, gastritis, epilepsy since 2011 receiving oxcarbazepine, terminal kidney disease all ongoing, ischemic heart disease in 2011 and 2015 (From 10Jun2011 to 06Jul2011 she was hospitalized due to acute myocardial infarction. from 30May2015 to 16Jun2015 she was hospitalized due to acute myocardial infarction without ST elevation with maximum troponin levels 0.345 ug/L), transient ischemic attack in 2010, heart failure -NYHA II, diarrhea from 24Oct2017 to 31Oct2017. The subject did not have any of the risk factors listed, she did not have obesity (BMI: 24.4) and she did not smoke. Concomitantly, the subject was taking pantoprazole (CONTROLOC) 20 mg orally once daily for gastritis, atorvastatin calcium (ATORIS) 20 mg orally once daily for hyperlipidemia, paricalcitol (ZEMPLAR) orally for hyperparathyroidismus, moxonidine total daily dose 0.6 mg with frequency twice daily orally since Feb2017 for hypertension, acetylsalicylic acid (ASPIRIN PROTECT) orally for cardiac protection, bisoprolol orally for cardiac protection, warfarin sodium (MARTEFARIN) orally for anticoagulation, carbohydrates nos/fats nos/minerals nos/proteins nos/ vitamins nos (NEPRO HP) orally for malnutrition, oxcarbazepine total daily dose 300 mg with frequency twice daily for epilepsy, all ongoing, urapidil (EBRANTIL) total daily dose 180 mg with frequency 3 times daily orally for hypertension, amlodipine besilate/ indapamide/perindopril arginine (TRIPLIXAM) total daily dose 10/2.5/10 mg orally once daily for hypertension. It was reported that was the subject was hospitalized on 24Oct2017 due to diarrhea. During hemodialysis the subject became confused with lateralization, hypotension occurred. Hospital discharge letter from the Department for infectious diseases included tests which showed brain CT on 26Oct2017: urgent brain CT showed left temporo-occipital hypodense lesion which corresponds to the postischemic brain malacia. On the edges of the lesion, hypodense parts could be gliosis, ischemia in development. Global atrophy. Periventricluar hypodense parts present due to neurodegenerative changes due to patient's age. No hemorrhage or tumor process. Neurological exams were done twice on 26Oct2017: Brain CT revealed an ischemic lesion. The patient was confused and disoriented. Control brain CT and control neurologic examination were recommended. On 27Oct2017: control exam showed the patient was in consciousness. CT confirmed ischemia in development. Discharge letter summary: the subject was treated in hospital for enterocolitis, she was treated with ciprofloxacin intravenously. On 26Oct2017, during regular hemodialysis, she developed hypotension, was disoriented and confused with sensorimotor dysphasia and the development of the lower right lip corner. She was examined by the neurologist, brain CT was done and due to development of neurological deficit which corresponded to ischemia in development which was confirmed by CT, the subject was transferred to neurological department on 27Oct2017. Neurology exam was performed, diagnosis: CVI suspect. On 01Dec2017, the event was amended to 'CVI', considered serious due to prolongation of hospitalization with an onset date of 26Oct2017. Diarrhea was added as an event and considered serious due to hospitalization. The onset date was reported as 24Oct2017. No action was taken with the study drug in response to the events. Urapidil and amlodipine besilate/ indapamide/perindopril arginine were stopped on an unspecified date. On 16Nov2017, the subject was discharged and considered recovered from the CVI and diarrhea. The investigator reported there was no reasonable possibility that the events, CVI and diarrhea, were related to the study drug or to any concomitant medication.

Follow-up (04Nov2017): Updates study drug details, medical history, concomitant medication details, event details, tests.

Follow-up (01Dec2017): Adds event 'diarrhea', deletes life-threatening as serious criteria for CVI, updates tests, hospitalization dates, outcome and confirms causality assessment.

Case Comment: Based on the information provided, there is no reasonable possibility that the reported event "CVI suspect" is related to the use of epoetin zeta. The hypotension during hemodialysis and the subject's underlying cerebro-cardiovascular conditions provided the most likely explanation to the event. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	JUL-2017	Activated partial thromboplastin time	0.97	
2	21-SEP-2017	Alanine aminotransferase	27 IU/l	36 10
3	21-SEP-2017	Aspartate aminotransferase	20 IU/l	30 8
4	24-OCT-2017	Aspartate aminotransferase	23 IU/l	30 8
5	25-OCT-2017	Band neutrophil count	15 %	
6	25-OCT-2017	Basophil count	0 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	21-SEP-2017	Blood albumin	35.6 g/l	52 35
8	21-SEP-2017	Blood alkaline phosphatase	91 IU/l	153 64
9	21-SEP-2017	Blood bilirubin	7 umol/l	20 3
10	24-OCT-2017	Blood bilirubin	10 umol/l	20 3
11	21-SEP-2017	Blood calcium	2.17 mmol/l	2.53 2.14
12	21-SEP-2017	Blood cholesterol	5.69 mmol/l	5
13	21-SEP-2017	Blood creatinine	668 umol/l	90 49
14	25-OCT-2017	Blood creatinine	448 umol/l	90 49
15	21-SEP-2017	Blood glucose	5.1 mmol/l	6.4 4.4
16	24-OCT-2017	Blood glucose	6.1 mmol/l	6.4 4.4
17	21-SEP-2017	Blood iron	9 umol/l	30 8
18	21-SEP-2017	Blood phosphorus	2 mmol/l	1.42 0.79
19	21-SEP-2017	Blood potassium	4.2 mmol	5.1 3.9
20	25-OCT-2017	Blood potassium	4.9 mmol	5.1 3.9
21	21-SEP-2017	Blood sodium	137 mmol/l	146 137
22	25-OCT-2017	Blood sodium	135 mmol/l	146 137
23	21-SEP-2017	Blood triglycerides	0.85 mmol/l	1.70
24	21-SEP-2017	Blood urea	22.9 mmol/l	8.3 2.8
25	25-OCT-2017	Blood urea	12.3 mmol/l	8.3 2.8
26	21-SEP-2017	Blood uric acid	446 umol/l	337 134
27		Body mass index	24.4	
28	21-SEP-2017	C-reactive protein	26.8 mg/l	5.0
29	OCT-2017	C-reactive protein	52.1 mg/l	5.0
30	24-OCT-2017	C-reactive protein	23.1 mg/l	5.0
31	25-OCT-2017	C-reactive protein	69.1 mg/l	5.0
32	26-OCT-2017	Computerised tomogram	Ischemic lesion	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
33	25-OCT-2017	Eosinophil count	0 %	
34	21-SEP-2017	Gamma-glutamyltransferase	60 IU/l	35 9
35	24-OCT-2017	Gamma-glutamyltransferase	61 IU/l	35 9
36	JUL-2017	Haematocrit	0.340	0.470 0.356
37	21-SEP-2017	Haematocrit	0.320	0.470 0.356
38	OCT-2017	Haematocrit	0.338	0.470 0.356
39	24-OCT-2017	Haematocrit	0.349	0.470 0.356
40	25-OCT-2017	Haematocrit	0.340	0.470 0.356
41	JUL-2017	Haemoglobin	10.8 g/dl	15.7 11.9
42	12-SEP-2017	Haemoglobin	11.2 g/dl	15.7 11.9
43	21-SEP-2017	Haemoglobin	10.4 g/dl	15.7 11.9
44	14-OCT-2017	Haemoglobin	11.0 g/dl	15.7 11.9
45	OCT-2017	Haemoglobin	10.7 g/dl	15.7 11.9
46	24-OCT-2017	Haemoglobin	11.1 g/dl	15.7 11.9
47	25-OCT-2017	Haemoglobin	10.8 g/dl	15.7 11.9
48	21-SEP-2017	High density lipoprotein	1.59 mmol/l	 1.20
49	JUL-2017	International normalised ratio	0.92	
50	OCT-2017	International normalised ratio	0.96	
51	21-SEP-2017	Iron binding capacity total	34.3 umol/l	75 36
52	21-SEP-2017	Iron binding capacity unsaturated	25.3 umol/l	59 26
53	21-SEP-2017	Low density lipoprotein	3.63 mmol/l	3
54	25-OCT-2017	Lymphocyte count	7 %	
55	JUL-2017	Mean cell haemoglobin	30.9 pg	33.9 27.4
56	21-SEP-2017	Mean cell haemoglobin	30.4 pg	33.9 27.4
57	OCT-2017	Mean cell haemoglobin	29.7 pg	33.9 27.4
58	24-OCT-2017	Mean cell haemoglobin	pg	33.9 27.4

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
59	JUL-2017	Mean cell haemoglobin concentration	318 g/l	345 320
60	21-SEP-2017	Mean cell haemoglobin concentration	325 g/l	345 320
61	OCT-2017	Mean cell haemoglobin concentration	317 g/l	345 320
62	24-OCT-2017	Mean cell haemoglobin concentration	318 g/l	345 320
63	25-OCT-2017	Mean cell haemoglobin concentration	318 g/l	345 320
64	JUL-2017	Mean cell volume	97.1	97.2 83.0
65	21-SEP-2017	Mean cell volume	93.6	97.2 83.0
66	OCT-2017	Mean cell volume	93.9	97.2 83.0
67	24-OCT-2017	Mean cell volume	93.3	97.2 83.0
68	25-OCT-2017	Mean cell volume	95	97.2 83.0
69	JUL-2017	Mean platelet volume	11.3	10.4 6.8
70	21-SEP-2017	Mean platelet volume	11.4	10.4 6.8
71	OCT-2017	Mean platelet volume	11.5	10.4 6.8
72	24-OCT-2017	Mean platelet volume	10.7	10.4 6.8
73	25-OCT-2017	Mean platelet volume	12.3	10.4 6.8
74	25-OCT-2017	Monocyte count	6 %	
75	JUL-2017	Platelet count	161 x10 9/l	424 158
76	21-SEP-2017	Platelet count	231 x10 9/l	424 158
77	OCT-2017	Platelet count	130 x10 9/l	424 158
78	24-OCT-2017	Platelet count	152 x10 9/l	424 158
79	25-OCT-2017	Platelet count	x10 9/l	424 158
80	24-OCT-2017	Procalcitonin	1.53 ng	
81	21-SEP-2017	Protein total	60.6 g/l	80 66
82	JUL-2017	Prothrombin time	1.18	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
83	OCT-2017	Prothrombin time	1.09	
84	JUL-2017	Red blood cell count	3.5 x10 12/l	5.08 3.86
85	21-SEP-2017	Red blood cell count	3.42 x10 12/l	5.08 3.86
86	OCT-2017	Red blood cell count	3.60 x10 12/l	5.08 3.86
87	24-OCT-2017	Red blood cell count	3.74 x10 12/l	5.08 3.86
88	25-OCT-2017	Red blood cell count	x10 12/l	5.08 3.86
89	25-OCT-2017	Red blood cell sedimentation rate	22	
90	JUL-2017	Red cell distribution width	14.7 %	15 9
91	21-SEP-2017	Red cell distribution width	14.3 %	15 9
92	OCT-2017	Red cell distribution width	14.9 %	15 9
93	24-OCT-2017	Red cell distribution width	15 %	15 9
94	25-OCT-2017	Red cell distribution width	15 %	15 9
95	21-SEP-2017	Serum ferritin	507.7	120 10
96	JUL-2017	Thrombin time	22.1	
97	21-SEP-2017	Transferrin	1.64 g/l	3.60 2
98	21-SEP-2017	Transferrin saturation	26 %	45 16
99	JUL-2017	White blood cell count	4.6 x10 9/l	9.7 3.4
100	21-SEP-2017	White blood cell count	5.0 x10 9/l	9.7 3.4
101	14-OCT-2017	White blood cell count	x10 9/l	9.7 3.4
102	OCT-2017	White blood cell count	5.1 x10 9/l	9.7 3.4
103	24-OCT-2017	White blood cell count	9.1 x10 9/l	9.7 3.4
104	25-OCT-2017	White blood cell count	7 x10 9/l	9.7 3.4

13. Relevant Tests

HDL-C/cholesterol (21Sep2017): 28% (normal low: 20%)
ECG (Jul2017): atrial fibrillation with average ventricular response 78/min
Brain CT (26Oct2017): urgent brain CT showed left temporo-occipital hypodense lesion which corresponds to the postischemic brain malacia. On the edges of the lesion, hypodense parts could be gliosis, ischemia in development. Global atrophy. Periventricluar hypodense parts present due to neurodegenerative changes due to patient's age. No hemorrhage or tumor process.

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	6000 IU, weekly; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	08-JUN-2017 / Ongoing; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) TRIPLIXAM (AMLODIPINE BESILATE, INDAPAMIDE, PERINDOPRIL ARGININE) ; Unknown

#7) ASPIRIN PROTECT (ACETYLSALICYLIC ACID) ; Ongoing

#8) BISOPROLOL (BISOPROLOL) ; Ongoing

#9) MARTEFARIN (WARFARIN SODIUM) ; Ongoing

#10) NEPRO HP (CARBOHYDRATES NOS, FATS NOS, MINERALS NOS, PROTEINS NOS, VITAMINS NOS) ; Ongoing

#11) OXCARBAZEPIN (OXCARBAZEPINE) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History NYHA II	Heart failure (Cardiac failure);
Unknown to Ongoing	Relevant Med History Therapy: atorvastatin	Hyperlipidemia (Hyperlipidaemia);
28-APR-2017 to Ongoing	Relevant Med History 3xweek	Haemodialysis (Haemodialysis);
Unknown	Relevant Med History	Non-smoker (Non-tobacco user);
16-MAY-2017 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
Unknown to Ongoing	Relevant Med History	Gastritis (Gastritis);
24-OCT-2017 to 31-OCT-2017	Relevant Med History	Diarrhoea (Diarrhoea);
2011 to Ongoing	Relevant Med History Therapy: oxcarbazepin	Epilepsy (Epilepsy);
Unknown to Ongoing	Relevant Med History	Renal disease (Nephropathy);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	BULGARIA	02	NOV	1931	85 Years	Male	85.00 kg	08	AUG	2017	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Myocardial infarction [Myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study for protocol EPOE-09-11, regarding subject BG025014.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # NA}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 2000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 06-MAR-2015 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CORDARONE (AMIODARONE HYDROCHLORIDE) ; Ongoing
#2) ADENURIC (FEBUXOSTAT) ; 2015 / Ongoing
#3) ARETA /01366402/ (LERCANIDIPINE HYDROCHLORIDE) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2005 to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease)
1968 to Ongoing	Relevant Med History	Hypertension (Hypertension)
	140/90 mmHg	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017502404

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 85-year-old Caucasian male subject started to receive epoetin zeta (RETACRIT) 2000 IU twice weekly on 06Mar2015 for renal anemia. The mean dose 1 of epoetin zeta was 2000 UI twice a week on 06Jun2017 with hemoglobin reported as "not applicable"; the mean dose 2 was 2000 UI twice a week on 04Jul2017 with hemoglobin reported as "not applicable". The date of last dose prior to event reported as 05Aug2017. The subject had a history of chronic kidney disease since 2005, hypertension since 1968 with "RR" 140/90 mmHg, chronic heart failure since 2000, obesity all ongoing, ischemic heart disease, recurrent atrial fibrillation, cancer, chronic gastrointestinal disease, gastrointestinal disorder, diarrhea, and gout. Type of dialysis reported as none (pre-dialysis). Three months prior to the event, dose was not changed. The subject was not on any other erythropoietin-stimulating agent (ESA). The subject had not experienced any thromboembolic event during treatment with any other ESA. Risk factor for thromboembolic events was reported as obesity (BMI-30). Concomitant medications included amiodarone (CORDARONE) 200 mg once daily for recurrent atrial fibrillation, febuxostat (ADENURIC) 1/2 of a 80 mg tablet every other day since 2015 for gout, and lercanidipine (ARETA) 10 mg twice daily for hypertension, all ongoing. The subject experienced a myocardial infarction on 08Aug2017. Seriousness criteria was reported as life-threatening, important medical event, and hospitalization involved (admission to hospital from 08Aug2017 to 11Aug2017). Additional information also included the following laboratory tests results: Hb (08Aug2017) 109 g/l (low); hematocrit (unknown date) 0.32 UL; RBC (unknown date) 3.63x10^12/l; WBC (unknown date) 12.8x10^9/l; CRP (unknown date) 13.6mg/l, and 28.4 mg/l; creatine kinase (unknown date) 83U/l, and 220 U/l; CK-MB (unknown date) 22 U/l, and 18 U/l; troponin I (08Aug2017) 0.45 ng/ml, and 2.69 ng/ml (high); ECG (unknown date) with result of "sinus rhythm Q wave in inferior loads ST depression and negative T wave V2-V4"; and echocardiography (unknown date) with result of "suppressed systolic function of left ventricle". Therapy with epoetin zeta was continued at the same dose. The subject was discharged from hospital on 11Aug2017. The subject recovered from the myocardial infarction on 11Dec2017. The investigator considered that there was not a reasonable possibility that the event myocardial infarction was related to the study medication or to a concomitant medication.

Follow-up (23Nov2017): new information from a contactable investigator includes: medical history and laboratory data updated; hospital admission dates; confirmation of event outcome.

Follow-up (08Dec2017): This is a follow-up report combining information from duplicate reports 2017502404 and 2017519235. The current and all subsequent follow-up information will be reported under manufacturer report number 2017502404. The new information includes: study drug details, seriousness criteria, medical history details, concomitant medication details, test details, hospitalization dates

Follow-up(13Dec2017) New reported information from same contactable investigator includes: outcome of adverse event reported as recovered on 11Dec2017. Action taken with suspect drug was reported as dose not changed.

Follow-up attempt completed. No expected further information.

Amendment: This follow-up report is being submitted to amend previously reported information: remove previously mentioned "As of 01Dec2017" in narrative.

Case Comment: In agreement with the investigator, the Company considered that there was not a reasonable possibility that the event myocardial infarction was related to the study medication. The subject's underlying cardiovascular diseases including hypertension, atrial fibrillation and advanced age are considered major risk factors for the event. The follow up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood creatine phosphokinase	83 uL	
2		Blood creatine phosphokinase	220 uL	
3		Blood creatine phosphokinase MB	22 uL	
4		Blood creatine phosphokinase MB	18 uL	
5		Blood pressure measurement	140/90 mmHg	
6		Body mass index	30	
7		C-reactive protein	13.6 mg/l	
8		C-reactive protein	28.4 mg/l	

Mfr. Control Number: 2017502404

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
9		Echocardiogram	Supressed systolic function	
		suppressed systolic function of left ventricle.		
10		Electrocardiogram	Sinus rhythm Q wave in	
		sinus rhythm Q wave in inferior loads ST depression and negative T wave V2-V4		
11		Haematocrit	0.32 uL	
12	08-AUG-2017	Haemoglobin	109 g/l	
13		Red blood cell count	3.63 x10 12/l	
14	08-AUG-2017	Troponin I	2.69 mg/ml	
15	08-AUG-2017	Troponin I	0.45 mg/ml	
16		White blood cell count	12.8 x10 9/l	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2000 to Ongoing	Relevant Med History	Chronic heart failure (Cardiac failure chronic);
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History Recurrent	Atrial fibrillation (Atrial fibrillation);
Unknown	Relevant Med History	Cancer (Neoplasm malignant);
Unknown	Relevant Med History	Diarrhoea (Diarrhoea);
Unknown	Relevant Med History Chronic gastrointestinal disease	Gastrointestinal disorder (Gastrointestinal disorder);
Unknown to Ongoing	Relevant Med History BMI - 30	Obesity (Obesity);
Unknown	Relevant Med History	Gout (Gout);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	08	JUL	1929	88 Years	Male	113.30 kg	26	JUL	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Apoplexy [Cerebrovascular accident]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study source for protocol EPOE-09-11, Center ID/Subject ID |GE012071.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 29-APR-2016 / 12-AUG-2016

19. THERAPY DURATION
#1) 106 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS (ACETYLSALICYLIC ACID) ; 28-NOV-2005 / Ongoing
#2) LYRICA (PREGABALIN) ; 20-JAN-2016 / Ongoing
#3) TORASEMID (TORASEMIDE) ; 09-FEB-2016 / Ongoing
#4) ALLOPURINOL (ALLOPURINOL) ; Unknown
#5) L-THYROXIN (LEVOTHYROXINE SODIUM) ; Unknown
#6) CANDESARTAN (CANDESARTAN) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)
Unknown	Relevant Med History	Ischemic heart disease (Myocardial ischaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017545676

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-JAN-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 88-years-old Caucasian male patient started to receive epoetin zeta, via an unspecified route of administration from 29Apr2016 to 12Aug2016 at 3000 IU for an unspecified indication. Medical history included hyperlipidemia, ischemic heart disease, diabetes mellitus, hypertension, chronic renal insufficiency grade III from an unknown date and unknown if ongoing. Risk factors: no obesity, no smoking, no Factor V Leiden, no Protein C or S deficiency, no Anthithrombin III deficiency, no Prothrombin G20210A mutation, no homocysteinemia, no recent surgery, no trauma, no significant and short term weight changes due to fluid retention/excretion, no vascular anomalies, no aneurysm, no immobilisation, no recent pregnancy, no positive family history; no transient ischemic attack, no peripheral arterial disease, no atrial fibrillation, no cancer, no chronic gastrointestinal disease, no diarrhea. Concomitant medication included ongoing acetylsalicylic acid (ASS) at 100 mg, 1x/day, 1-0-0-0 from 28Nov2005; ongoing pregabalin (LYRICA) at 50 mg, 2x/day from 20Jan2016; ongoing torasemide (TORASEMID; strength: 10 mg) at 10 mg, 2x/day, 1-1-0-0 from 09Feb2016; allopurinol (strength: 300 mg) at 150 mg, 1x/day; levothyroxine sodium (L-THYROXIN; strength: 75 ug) at 75 ug, 1x/day; candesartan (strength: 8 mg) at 8 mg, 2x/day; pyridostigmine bromide (KALYMIN); clopidogrel (strength: 75 mg) at 75 mg, 1x/day; insulin glargine (TOUJEO) subcutaneously at 24 IU, 1x/day for diabetes mellitus; insulin lispro (HUMALOG) for diabetes mellitus. The patient experienced apoplexy (cerebrovascular accident) (hospitalization) on 26Jul2017 with outcome of recovered on 17Aug2017. The patient was hospitalized for apoplexy from 26Jul2017 to 17Aug2017. Relevant information from attached physician's letter: they took over the patient on 26Jul2017 for geriatric complex treatment. The reason for admission was a brain ischemic insult with hemiparesis right. Patient underwent cardiac catheter examination. The patient received a DES [drug-eluting stent] and a pacemaker. We first continued antibiotic therapy with Cotrim 960 mg until 28Jul2017. The patient additionally received allopurinol, L-Thyroxin, candesartan, torasemide, pregabalin, Kalymin retard, clopidogrel and ASS 100 mg. Diabetes mellitus was treated with Toujeo and Humalog insulin. Insulin had to be reduced due to hypoglycemic blood glucose values and the plan was modified accordingly, patient reported that he eats less at hospital than at home. After withdrawal of Lyrica patient complained increasingly about motion-dependent thoracic pain on the left sideWe started treatment with Lyrica with reduced dose again. A chronic renal insufficiency with grade III is known. The patient was under nephrological therapy. The thyroid function is euthyroid. Discharge medication included: Toujeo at 24 IU subcutaneous in the evening, Humalog insulin according to plan with reduced dose, Lyrica 25 mg 1 in the morning and in the evening, Mestinon retard 180 mg 0.5 in the morning, Pipamperon 40 mg 0.5 at night, allopurinol 300 mg 0.5 in the morning, L-Thyroxin 75 ug 1 in the morning, candesartan 8 mg 1 in the morning and in the evening, Torem 10 mg 1 in the morning and at noon, clopidogrel 75 mg (over 1 year after heart catheter examination) 1 in the morning, Aspirin protect 100 mg (lifetime) 1 in the morning. The patient underwent lab tests which included blood pressure: normal on unknown date, ECG at rest: atrial stimulated pacemaker rhythm on unknown date, x-ray: distinct degenerative changes of thoracic spine on unknown date. The action taken in response to the event for epoetin zeta was post-therapy. Therapeutic measures were taken as a result of apoplexy. The event was assessed as unrelated to study drug and concomitant medication.

Follow-up (22Jan2018): New information received from investigator includes: medical history, lab data, concomitant drugs, hospitalization information, treatment.

Case Comment: The event was considered as unrelated to study drug and concomitant medication.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood pressure measurement	normal	
2		Electrocardiogram	atrial stimulated pacemaker rhythm	
3		X-ray	distinct degenerative changes of thoracic spine	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) KALYMIN (PYRIDOSTIGMINE BROMIDE) ; Unknown

#8) CLOPIDOGREL (CLOPIDOGREL) ; Unknown

#9) TOUJEO (INSULIN GLARGINE) ; Unknown

#10) HUMALOG (INSULIN LISPRO) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown 27-Aug-2020 04:52	Relevant Med History	Diabetes mellitus (Diabetes mellitus);

Mfr. Control Number: 2017545676

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History grade III	Chronic renal insufficiency (Chronic kidney disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1929	88 Years	Male	76.00 kg	05	DEC	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

humoral shock [Shock]
NSTEMI [Acute myocardial infarction]
NSTEMI [Acute myocardial infarction]
Triple vessel disease [Coronary artery disease]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 27-APR-2018
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 3000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 28-JUL-2015 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) IS 5 MONO RATIOPHARM (ISOSORBIDE MONONITRATE) ; 2017 / Ongoing
#2) JANUVIA (SITAGLIPTIN PHOSPHATE) ; 2017 / Ongoing
#3) TORASEMIDE (TORASEMIDE) ; 2017 / Ongoing
#4) ASS (ACETYLSALICYLIC ACID) ; 2017 / Ongoing
#5) HCT (HYDROCHLOROTHIAZIDE) ; 2017 / Ongoing
#6) CALCIUMACETATE NEFRO (CALCIUM ACETATE) ; 2017 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
2004 to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus)
2004 to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017546018

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-APR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a report from a non-interventional study source for protocol EPOE-09-11. This 88-year-old male subject started on epoetin zeta (RETACRIT) 3000 IU subcutaneously once weekly from 28Jul2015 to an unspecified date, then 3000 IU once weekly from 15Feb2018 to 15Mar2018, then 2000 IU once weekly from 20Mar2018 for the study indication of renal anemia. The subject's medical history included type 2 diabetes mellitus, diabetic nephropathy, diabetic retinopathy and heart failure, all since 2004, coronary heart disease since Sep2004, atrial fibrillation since 2014, and hypertension since 2014, all ongoing, and a myocardial infarction in 2004; additionally, the subject had received hemodialysis. It's also reported that relevant concomitant and past diseases: atrial fibrillation: no. Concomitantly, the subject was taking isosorbide mononitrate (IS 5 MONO RATIOPHARM) 60 mg, sitagliptin phosphate (JANUVIA) 25 mg, torasemide 200 mg, acetylsalicylic acid (ASS) and hydrochlorothiazide (HCT) 25 mg, all once daily since 2017, calcium acetate (CALCIUMACETATE NEFRO) 700 mg three times daily since 2017, pravastatin 40 mg once daily since 2008, alfacalcidol (BONDIOL) 0.25 ug once daily since 2014, enoxaparin sodium (CLEXANE) subcutaneously on dialysis days since 2016, molsidomine (CORVATON) at 8 mg once daily (schedule: 1-0-0) since Dec2017, amlodipine besilate (AMLODIPIN) at 5mg once daily (schedule: 1-0-0) since 2018, all ongoing, and glyceryl trinitrate (NITROLINGUAL SPRAY) via respiratory inhalation as needed since 2017. Prior to the event, the routine lab data on 13Jun2017 included beta 2 globulin 7.6% (range 3.2-6.5), high density lipoprotein (HDL) 36 mg/dl (range > 45), low density lipoprotein (LDL) 53 mg/dl. On 12Sep2017, hematocrit 37.8 % (range 39.4 - 53.0), hemoglobin 12.7 g/dl (range 12.6 - 17.4), red blood cell count (RBC) 4.05x10 6/mm3 (range 4.02 - 5.86) and white blood cell count (WBC) 8.65x10 9/l (range 4.06 - 11.9). On 10Oct2017, uric acid 7.1 mg/dl (high range <7.0), C-reactive protein (CRP) 5.8 mg/l (high range <5.0), hematocrit 36.9 %, hemoglobin 12.6 g/l, RBC 3.95x10 6/mm3 and WBC 7.54x10 9/l. On 14Nov2017, calcium 1.07 mmol/l and 2.21 mmol/l (range 2.20 - 2.55), creatinine 7.74 mg/dl (high range <1.30), phosphate 4.71 mg/dl (range 2.51 - 4.49), sodium 134 mmol/l, urea 136 mg/dl (high range <50), CRP 3.2 mg/l, glomerular filtration rate (GFR) 6 ml/min (low range >90), hematocrit 36.9 %, hemoglobin 12.5 g/dl, RBC 3.93x10 6/mm3 and WBC 6.95x10 9/l. The first event occurred on 05Dec2017 when the subject was diagnosed with non-ST segment elevation myocardial infarction (NSTEMI) with suspect coronary heart disease with moderately impaired systolic left ventricular function that required him to be hospitalized from 05Dec2017 to 07Dec2017. He received a new medication: molsidomin (CORVATON) once daily. The subject was considered as recovered on 07Dec2017. Prior to this first event, the subject last took epoetin zeta on 05Dec2017. Lab data on 12Dec2017 included beta 2 globulin 7.50%, calcium 1.03 mmol/l and 2.13 mmol/l, creatinine 8.10 mg/dl, phosphate 5.30 mg/dl, sodium 136 mmol/l, urea 171 mg/dl, uric acid 8.1 mg/dl, CRP 2.7 mg/l, GFR 5 ml/min, hematocrit 35.2%, hemoglobin 12.2 g/dl, HDL 43 mg/dl, LDL 50 mg/dl, RBC 3.78x10 6/mm3, and WBC 7.20x10 9/l. The dose of epoetin zeta was changed on 15Feb2018 with new dose being 2000 IU once weekly. Hemoglobin prior to the dose change was 12.7 g/dl on 13Feb2018 and afterwards was 12.0 g/dl on 13Mar2018. The subject did not receive any other erythropoietin stimulating substances. New lab data included: Hemoglobin (normal range: 12.6-17.4) on 09Jan2018 at 12.2 g/dl, on 13Feb2018 at 12.7 g/dl and on 13Mar2018 at 12.0 g/dl. Hematocrit (normal range: 39.4-53.0) on 09Jan2018 at 35.0 %, on 13Feb2018 at 37.2 % and on 13Mar2018 at 35.2 %. Erythrocytes (RBC) (normal range: 4.02-5.86) on 09Jan2018 at 3.75 /pl, on 13Feb2018 at 3.95 /pl and on 13Mar2018 at 3.78 /pl. C-reactive protein (normal range: < 5.0) on 09Jan2018 at 5.1 mg/l, on 13Feb2018 at 2.6 mg/l and on 13Mar2018 at 3.3 mg/l. Leucocytes (WBC) (normal range: 4.06-11.9) on 09Jan2018 at 7.24 /nl, on 13Feb2018 at 7.62 /nl and on 13Mar2018 at 7.37 /nl. The second event occurred on 20Mar2018 when the subject was diagnosed with NSTEMI in context of coronary heart disease with urgent indication for aorto-coronary venous bypass (ACVB) operation that required him to be hospitalized on 20Mar2018 until he was transferred to a cardiologic hospital on 31Mar2018. The following medication was taken after the event: ramipril 1.25 mg once daily, bisoprolol 2.5 mg once daily, molsidomin 8 mg once daily, ASS 100 mg once daily. Epoetin zeta has been reduced because hemoglobin level was 12.7 on 13Feb2018. The reason was not a SAE. The NSTEMI lasted from 20Mar2018 to 31Mar2018. The subject suffered from a 3-vessel-disease from 31Mar2018 due to which he has been transferred to a cardiac unit. The subject experienced serious event humorous shock on 27Apr2018 with fatal outcome. The subject passed away on 27Apr2018. No autopsy was performed.
Additional lab tests included: Hemoglobin values out of range (unit: g/dl), started from 14Jun2017 until 24Oct2018: 9.1 (14Jun2017), 10.8 (10Jul2017), 11.1 (07Aug2018), 11.3 (22Jan2018), 10.8 (12Feb2018), 12.2 (12Mar2018), 11.8 (07May2018), 7.9 (28Jun2018), 8.4 (16Jul2018), 8.6 (22Aug2018), 9.1 (04Sep2018), 10.2 (24Sep2018), 9.8 (15Oct2018), 10.3 (24Oct2018). Hematocrit values out of range (unit: %), started from 14Jun2017 until 24Oct2018: 27.0 (14Jun2017), 33.0(10Jul2017), 33.1 (07Aug2018), 38.3 (13Nov2018), 33.5 (22Jan2018), 32.5 (12Feb2018), 37.0 (12Mar2018), 34.9 (07May2018), 24.5 (28Jun2018), 25.8 (16Jul2018), 26.3 (22Aug2018), 28.6 (04Sep2018), 31.7 (24Sep2018), 30.4 (15Oct2018), 30.8 (24Oct2018). Erythrocytes out of range (unit: x10 6/mm3), started from 14Jun2017 until 24Oct2018: 2.89 (14Jun2017), 3.34(10Jul2017), 3.47 (07Aug2018), 3.79 (13Nov2018), 3.22 (22Jan2018), 3.14 (12Feb2018), 3.57 (12Mar2018), 3.39 (07May2018), 2.25 (28Jun2018), 2.39 (16Jul2018), 2.48 (22Aug2018), 2.72 (04Sep2018), 3.09 (24Sep2018), 3.07 (15Oct2018), 3.22 (24Oct2018). CRP values out of range (unit: mg/l), started from 14Jun2017 until 15Oct2018: 49 (14Jun2017), 7.9(10Jul2017), 164 (02Aug2017), 86 (07Aug2017), 12 (11Sep2017), 10 (13Nov2017), 96 (22Jan2018), 268 (09Feb2018), 79 (12Feb2018), 25 (12Mar2018), 29 (07May2018), 41 (28Jun2018), 90 (10Jul2018), 83 (22Aug2018), 68 (04Sep2018), 62 (15Oct2018). Leucocytes out of range on 07Aug2017: 12.1 x10 9/l. No action was taken with epoetin zeta in response to the events, the last action taken in response to the events for epoetin zeta was not applicable. The outcome of event NSTEMI was recovered on 07Dec2017, of event second NSTEMI was recovered on 31Mar2018, of triple vessel disease was not recovered, of the event humorous shock was fatal.
The investigator reported that there was not a reasonable possibility that the event, NSTEMI, was related to the study drug or to any concomitant medication. The reporter assessed the event NSTEMI, as serious as it caused hospitalization and unrelated to study medication. The investigator assessed the SAE Triple vessel disease to be unrelated to the study drug and to the concomitant drugs. No causality assessment was provided for the new fatal event humorous shock.

The reporter's assessment of the causal relationship of the event humorous shock with suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Follow-up (29Dec2017): New information received included subject's age, action taken, and lab data.

Follow-up (18Jan2018): Updates suspect product details, history and tests.

Follow-up (21Mar2018): New information received from the investigator included: updated concomitant medications (Corvaton and Amlodipin), event details (event outcome and date).

Follow-up (20Apr2018): Added another event of NSTEMI on 20Mar2018 with hospitalization, another dosage for the study therapy and new lab data.

Follow-up (19Dec2018): New information received from the investigator included: Lab data added.

Follow-up (08Jan2019): New information received from the investigator included: study drug therapy dates and dosage regimen, event details, death detail, and treatment.

Follow-up (28Feb2019): New information received from the investigator adds serious adverse event "three vessel disease", clarified epoetin dosing regimen.

Follow-up (08Apr2019): New information received from the investigator included: serious fatal event humorous shock added, triple vessel disease outcome updated and causality provided, epoetin dosing regimen confirmed.

Follow-up (12Apr2019): new information received from investigator includes: information about autopsy, epoietin zeta dose units provided.

Follow-up (23Apr2019): New information received from investigator via CRO includes: Numerous shock does not exist and humoral shock is really the cause of death and not an AESI.

Case Comment: Based on the available information and in agreement with the investigator, the Company considered there was not a reasonable possibility that the two episodes of NSTEMI and three vessel disease, were related to the study drug epoetin zeta. There is not a reasonable possibility that the drug contributed to occurrence of the event: serious fatal event humoral shock. The underlying multiple risk factors including diabetes mellitus, coronary heart disease, atrial fibrillation provided the most likely explanation to the development of events.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	13-JUN-2017	Beta 2 globulin	7.60 %	6.50 3.20
2	12-DEC-2017	Beta 2 globulin	7.50 %	6.50 3.20
3	14-NOV-2017	Blood calcium	2.21 mmol/l	2.55 2.20
4	14-NOV-2017	Blood calcium	1.07 mmol/l	
5	12-DEC-2017	Blood calcium	1.03 mmol/l	
6	12-DEC-2017	Blood calcium	2.13 mmol/l	2.55 2.20
7	14-NOV-2017	Blood creatinine	7.74 mg/dl	<1.30
8	12-DEC-2017	Blood creatinine	8.10 mg/dl	<1.30
9	14-NOV-2017	Blood phosphorus	4.71 mg/dl	4.49 2.51
10	12-DEC-2017	Blood phosphorus	5.30 mg/dl	4.49 2.51
11	14-NOV-2017	Blood sodium	134 mmol/l	
12	12-DEC-2017	Blood sodium	136 mmol/l	
13	14-NOV-2017	Blood urea	136 mg/dl	<50

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
14	12-DEC-2017	Blood urea	171 mg/dl	<50
15	10-OCT-2017	Blood uric acid	7.1 mg/dl	<7.0
16	12-DEC-2017	Blood uric acid	8.1 mg/dl	<7.0
17	14-JUN-2017	C-reactive protein	49 mg/l	<5.0
18	10-JUL-2017	C-reactive protein	7.9 mg/l	<5.0
19	02-AUG-2017	C-reactive protein	164 mg/l	<5.0
20	07-AUG-2017	C-reactive protein	86 mg/l	<5.0
21	11-SEP-2017	C-reactive protein	12 mg/l	<5.0
22	10-OCT-2017	C-reactive protein	5.8 mg/l	<5.0
23	13-NOV-2017	C-reactive protein	10 mg/l	<5.0
24	14-NOV-2017	C-reactive protein	3.2 mg/l	<5.0
25	12-DEC-2017	C-reactive protein	2.7 mg/l	<5.0
26	09-JAN-2018	C-reactive protein	5.1 mg/l	<5.0
27	22-JAN-2018	C-reactive protein	96 mg/l	<5.0
28	09-FEB-2018	C-reactive protein	268 mg/l	<5.0
29	12-FEB-2018	C-reactive protein	79 mg/l	<5.0
30	13-FEB-2018	C-reactive protein	2.6 mg/l	<5.0
31	12-MAR-2018	C-reactive protein	25 mg/l	<5.0
32	13-MAR-2018	C-reactive protein	3.3 mg/l	<5.0
33	07-MAY-2018	C-reactive protein	29 mg/l	<5.0
34	28-JUN-2018	C-reactive protein	41 mg/l	<5.0
35	10-JUL-2018	C-reactive protein	90 mg/l	<5.0
36	22-AUG-2018	C-reactive protein	83 mg/l	<5.0
37	04-SEP-2018	C-reactive protein	68 mg/l	<5.0
38	15-OCT-2018	C-reactive protein	62 mg/l	<5.0
39	14-NOV-2017	Glomerular filtration rate	6 ml/min	>90

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
40	12-DEC-2017	Glomerular filtration rate	5 ml/min	>90
41	14-JUN-2017	Haematocrit	27.0 %	53.0 39.4
42	10-JUL-2017	Haematocrit	33.0 %	53.0 39.4
43	07-AUG-2017	Haematocrit	33.1 %	53.0 39.4
44	12-SEP-2017	Haematocrit	37.8 %	53.0 39.4
45	10-OCT-2017	Haematocrit	36.9 %	53.0 39.4
46	13-NOV-2017	Haematocrit	38.3 %	53.0 39.4
47	14-NOV-2017	Haematocrit	36.9 %	53.0 39.4
48	12-DEC-2017	Haematocrit	35.2 %	53.0 39.4
49	09-JAN-2018	Haematocrit	35.0 %	53.0 39.4
50	22-JAN-2018	Haematocrit	33.5 %	53.0 39.4
51	12-FEB-2018	Haematocrit	32.5 %	53.0 39.4
52	13-FEB-2018	Haematocrit	37.2 %	53.0 39.4
53	12-MAR-2018	Haematocrit	37.0 %	53.0 39.4
54	13-MAR-2018	Haematocrit	35.2 %	53.0 39.4
55	07-MAY-2018	Haematocrit	34.9 %	53.0 39.4
56	28-JUN-2018	Haematocrit	24.5 %	53.0 39.4
57	16-JUL-2018	Haematocrit	25.8 %	53.0 39.4
58	22-AUG-2018	Haematocrit	26.3 %	53.0 39.4
59	04-SEP-2018	Haematocrit	28.6 %	53.0 39.4
60	24-SEP-2018	Haematocrit	31.7 %	53.0 39.4
61	15-OCT-2018	Haematocrit	30.4 %	53.0 39.4
62	24-OCT-2018	Haematocrit	30.8 %	53.0 39.4
63	14-JUN-2017	Haemoglobin	9.1 g/dl	17.4 12.6
64	10-JUL-2017	Haemoglobin	10.8 g/dl	17.4 12.6
65	07-AUG-2017	Haemoglobin	11.1 g/dl	17.4 12.6

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
66	12-SEP-2017	Haemoglobin	12.7 g/dl	17.4 12.6
67	10-OCT-2017	Haemoglobin	12.6 g/dl	17.4 12.6
68	14-NOV-2017	Haemoglobin	12.5 g/dl	17.4 12.6
69	12-DEC-2017	Haemoglobin	12.2 g/dl	17.4 12.6
70	09-JAN-2018	Haemoglobin	12.2 g/dl	17.4 12.6
71	22-JAN-2018	Haemoglobin	11.3 g/dl	17.4 12.6
72	12-FEB-2018	Haemoglobin	10.8 g/dl	17.4 12.6
73	13-FEB-2018	Haemoglobin	12.7 g/dl	17.4 12.6
74	12-MAR-2018	Haemoglobin	12.2 g/dl	17.4 12.6
75	13-MAR-2018	Haemoglobin	12.0 g/dl	17.4 12.6
76	07-MAY-2018	Haemoglobin	11.8 g/dl	17.4 12.6
77	28-JUN-2018	Haemoglobin	7.9 g/dl	17.4 12.6
78	16-JUL-2018	Haemoglobin	8.4 g/dl	17.4 12.6
79	22-AUG-2018	Haemoglobin	8.6 g/dl	17.4 12.6
80	04-SEP-2018	Haemoglobin	9.1 g/dl	17.4 12.6
81	24-SEP-2018	Haemoglobin	10.2 g/dl	17.4 12.6
82	15-OCT-2018	Haemoglobin	9.8 g/dl	17.4 12.6
83	24-OCT-2018	Haemoglobin	10.3 g/dl	17.4 12.6
84	13-JUN-2017	High density lipoprotein	36 mg/dl	>45
85	12-DEC-2017	High density lipoprotein	43 mg/dl	>45
86	13-JUN-2017	Low density lipoprotein	53 mg/dl	
87	12-DEC-2017	Low density lipoprotein	50 mg/dl	
88	14-JUN-2017	Red blood cell count	2.89 x10 6/mm3	5.86 4.02
89	10-JUL-2017	Red blood cell count	3.34 x10 6/mm3	5.86 4.02
90	07-AUG-2017	Red blood cell count	3.47 x10 6/mm3	5.86 4.02
91	12-SEP-2017	Red blood cell count	4.05 x10 6/mm3	5.86 4.02

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
92	10-OCT-2017	Red blood cell count	3.95 x10 6/mm3	5.86 4.02
93	13-NOV-2017	Red blood cell count	3.79 x10 6/mm3	5.86 4.02
94	14-NOV-2017	Red blood cell count	3.93 x10 6/mm3	5.86 4.02
95	12-DEC-2017	Red blood cell count	3.78 x10 6/mm3	5.86 4.02
96	09-JAN-2018	Red blood cell count	3.75 x10 6/mm3	5.86 4.02
97	22-JAN-2018	Red blood cell count	3.22 x10 6/mm3	5.86 4.02
98	12-FEB-2018	Red blood cell count	3.14 x10 6/mm3	5.86 4.02
99	13-FEB-2018	Red blood cell count	3.95 x10 6/mm3	5.86 4.02
100	12-MAR-2018	Red blood cell count	3.57 x10 6/mm3	5.86 4.02
101	13-MAR-2018	Red blood cell count	3.78 x10 6/mm3	5.86 4.02
102	07-MAY-2018	Red blood cell count	3.39 x10 6/mm3	5.86 4.02
103	28-JUN-2018	Red blood cell count	2.25 x10 6/mm3	5.86 4.02
104	16-JUL-2018	Red blood cell count	2.39 x10 6/mm3	5.86 4.02
105	22-AUG-2018	Red blood cell count	2.48 x10 6/mm3	5.86 4.02
106	04-SEP-2018	Red blood cell count	2.72 x10 6/mm3	5.86 4.02
107	24-SEP-2018	Red blood cell count	3.09 x10 6/mm3	5.86 4.02
108	15-OCT-2018	Red blood cell count	3.07 x10 6/mm3	5.86 4.02
109	24-OCT-2018	Red blood cell count	3.22 x10 6/mm3	5.86 4.02
110	07-AUG-2017	White blood cell count	12.1 x10 9/l	11.9 4.06
111	12-SEP-2017	White blood cell count	8.65 x10 9/l	11.9 4.06
112	10-OCT-2017	White blood cell count	7.54 x10 9/l	11.9 4.06
113	14-NOV-2017	White blood cell count	6.95 x10 9/l	11.9 4.06
114	12-DEC-2017	White blood cell count	7.20 x10 9/l	11.9 4.06
115	09-JAN-2018	White blood cell count	7.24 x10 9/l	11.9 4.06
116	13-FEB-2018	White blood cell count	7.62 x10 9/l	11.9 4.06
117	13-MAR-2018	White blood cell count	7.37 x10 9/l	11.9 4.06

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	3000 IU, weekly; Unknown	renal anemia (Nephrogenic anaemia)	15-FEB-2018 / 15-MAR-2018; 29 days
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #3	2000 IU, weekly; Unknown	renal anemia (Nephrogenic anaemia)	20-MAR-2018 / Unknown; Unknown
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #4	UNK; Unknown	renal anemia (Nephrogenic anaemia)	Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) PRAVASTATIN (PRAVASTATIN) ; 2008 / Ongoing

#8) BONDIOL (ALFACALCIDOL) ; 2014 / Ongoing

#9) CLEXANE (ENOXAPARIN SODIUM) ; 2016 / Ongoing

#10) CORVATON (MOLSIDOMINE) ; DEC-2017 / Ongoing

#11) AMLODIPIN (AMLODIPINE BESILATE) ; 2018 / Ongoing

#12) NITROLINGUAL SPRAY (GLYCERYL TRINITRATE) ; 2017 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2004 to Ongoing	Relevant Med History	Diabetic retinopathy (Diabetic retinopathy);
2004 to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
SEP-2004 to Ongoing	Relevant Med History	Coronary heart disease (Coronary artery disease);
2014 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
2014 to Ongoing	Relevant Med History	Hypertension (Hypertension);
2004 to 2004	Relevant Med History	Myocardial infarction (Myocardial infarction);
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		AUG	1932	84 Years	Female	87.50 kg	05	AUG	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-interventional Study, Protocol EPOE-09-11, regarding subject GE0930141.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) EPOETIN ZETA (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 IU, 1x/ week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 05-JAN-2015 / Ongoing

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
13-FEB-2012 to Ongoing	Relevant Med History	Renal failure (Renal failure)
Unknown to Ongoing	Relevant Med History	Hemodialysis (Haemodialysis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018023376

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-JUN-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2018023376

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 84-year-old female patient started to receive epoetin zeta (RETACRIT) 4000 IU subcutaneously once per week from 05Jan2015 and ongoing for renal anemia. Lot number was not available. The most recent dose prior to the event was on 04Aug2017. The patient was on hemodialysis. The patient previously received epoetin theta (BIOPOIN) 12000 IU/week from 06Jul2012 to 03Jun2015 with her hemoglobin in the range of 7.5-14.8 g/dl for renal anemia and had no thromboembolic event. There were no thromboembolic events under treatment with other erythropoietin-stimulating medicines. Her medical history included renal failure from 13Feb2012, hypertension, diabetes mellitus, and adipositas (BMI 31.05 kg/m2), hemodialysis, all ongoing. No concomitant medications were provided. The patient was admitted to the hospital on 02Aug2017 due to choledocholithiasis (not reported as an event). During her hospital stay, she experienced chest pain, and on 05Aug2017, was diagnosed with a non ST segment elevation myocardial infarction (NSTEMI), considered serious due to hospitalization. Chest pain was considered symptom of the event NSTEMI. Tests on 05Aug2017 included troponin of 1248 pg/ml (range unknown). The patient was treated with heparin and acetylsalicylate lysine (ASPISOL). No action was taken with epoetin zeta in response to the event. The patient was considered recovered on 09Aug2017. On dosing date 15May2017, her hemoglobin was 12.3 g/d; and on 03Jul2017, 13.1 g/dl (reference range: from 12.0 to 16.0 g/dl). The investigator reported the event of NSTEMI was unrelated to the study drug or to any concomitant medication.

Follow-up (31Jan2018): New information received from the investigator includes: patient age, study drug batch number (unavailable) and event detail, confirms choledocholithiasis was not considered an event.

Follow-up (09Feb2018): Updates history, past drug history, study drug details, and tests.

Follow-up (30May2018): New information received from the investigator includes: reference range for hemoglobin (from 12.0 to 16.0 g/dl).

Follow-up (28Jun2018): New information received from the contactable investigator includes: confirms chest pain as symptom of event.

Case Comment: Based on the information currently provided, the company concurs with the causality assessment provided by the investigator, considering the event of NSTEMI was unrelated to the study drug. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	15-MAY-2017	Haemoglobin	12.3 g/dl	16.0 12.0
2	03-JUL-2017	Haemoglobin	13.1 g/dl	16.0 12.0
3	05-AUG-2017	Troponin	1.248 ng/ml	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus);
Unknown to Ongoing	Relevant Med History BMI 31.05 kg/m2	Adipositas (Obesity);
06-JUL-2012 to 03-JUN-2015	Past Drug Event	BIOPOIN (BIOPOIN); Drug Indication: Renal anemia (Nephrogenic anaemia), Drug Reaction: No adverse event (No adverse event) 12000 IU/ week; with hemoglobin range of 7.5 - 14.8 g/dl

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	10	NOV	1944	73 Years	Female	65.00 kg	26	NOV	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pulmonitis [Pneumonitis]
NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study source for Protocol EPOE-09-11 for Center ID 059, Subject ID 0009.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 22-DEC-2017
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 4000 IU, c (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) anemia in kidney failure (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 11-AUG-2015 / 20-NOV-2017

19. THERAPY DURATION
#1) 833 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN (INSULIN) ; Unknown
#2) CARDIOASPIRIN (ACETYLSALICYLIC ACID) ; Unknown
#3) PLAVIX (CLOPIDOGREL BISULFATE) ; Unknown
#4) BISOPROLOL (BISOPROLOL) ; Unknown
#5) AMLODIPINE (AMLODIPINE) ; Unknown
#6) LASIX /00032601/ (FUROSEMIDE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1974 to Ongoing	Relevant Med History	Type II diabetes mellitus (Type 2 diabetes mellitus)
2000 to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018031606

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-MAR-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old, Caucasian, female subject started to receive EPOETIN ZETA (Epoetin Zeta, Solution for injection) subcutaneously from 11Aug2015 to 20Nov2017, for anemia in kidney failure. The most recent dose before the events was 4000 IU, cyclic (1 vial every 10 days). The patient was not exposed to any other erythropoietin-stimulating agent(ESA). Medical history included ongoing diabetes mellitus II from 1974, ongoing hypertension from 2000, coronary heart disease, ongoing hyperlipidemia, ischaemic heart disease, peripheral arterial disease (from 2006/2007), and atherosclerosis. No risk factors for thromboembolic events. Concomitant medications included insulin (INSULIN) for diabetes mellitus, acetylsalicylic acid (CARDIOASPIRIN) for coronary artery disease, clopidogrel bisulfate (PLAVIX) for coronary artery disease, bisoprolol (BISOPROLOL) for coronary artery disease and cardio protection, amlodipine (AMLODIPINE) for hypertension, furosemide (LASIX) for hypertension, valsartan (TAREG) for hypertension, acetylsalicylic acid (ASPIRIN) for atherosclerosis, and insulin glulisine (APIDRA) for diabetes. It was reported that the mean dose was 4000 IU on 11Sep2017, and no changes were done within 3 months prior to the events. On 26Nov2017 the subject developed pulmonitis. The seriousness criteria for this event were hospitalization and death. On 27Nov2017, the subject had a non-ST evaluated myocardial infarction (NSTEMI). The seriousness criteria for this event was hospitalization; patient was admitted to hospital because of NSTEMI from to 27Nov2017 to 21Dec2017, and the event was also reported as threatening. The patient underwent lab tests and procedures which included hemoglobin: 11.9 g/dl on an unspecified date; basophils: 0.02 x10 3/mm3 (reference values: 0-0.12) and 0.2 %, creatinine: 3.30 mg/dl (reference values: 0.50-1), glucose: 103 mg/dl (reference values: 60-99), sodium: 144 mEq/l (reference values: 134-146), urea: 179 mg/dl (reference values: 10-50), eosinophils: 0.34 x10 3/mm3 (reference values: 0-0.57) and 3.7 %, HbA1c: 55 mmol/mol (reference values: 20 - 38) and 7.2 % (reference values: 4-5.6), hematocrit:37.3 % (reference values: 35-45), hemoglobin; 11.8 g/dl (reference values: 12-14.9), lymphocytes: 3.37 x10 3/mm3 (reference values: 1.50-3.93) and 36.8 %, MCH: 29.6 pg (reference values: 25-33), MCHC: 31.6 g/dl (reference values: 30.5-35), MCV: 93.5 fL (reference values: 80.0-98.0), MPV: 13.1 fL (reference values: 9.1 - 13.1), monocytes: 0.77 x10 3/mm3 (reference values: 0.14-0.86) and 8.4 %, neutrophils: 4.66 x10 3/mm3 (reference values: 2-8) and 50.9 %, platelet: 231 x10 3/mm3 (reference values: 150-450), RBC: 3.99 x10 6/mm3 (reference values: 3.84-5.10), RDW-CV: 14.5 % (reference values: 11-16), and WBC: 9.16 x10 3/mm3 (reference values: 4-10) on 07Sep2017; and chest scan on 26Nov2017 that showed pulmonitis. Additional drugs taken by subject for pulmonitis included: Linezolid oral from 04Dec2017, Levofloxacin (LEVOXACIN) oral from 01Dec2017, Cefazolin intravenous from 26Nov2017 and Meropenem intravenous from 20Dec2017. The outcome of the event for NSTEMI was not recovered and for pneumonitis was fatal. The action taken was not applicable. The patient died on 22Dec2017. The cause of death was reported as: NSTEMI in progress and pulmonitis. An autopsy was not performed. The investigator considered that the relationship of the event to treatment with Epoetin Zeta and concomitant medications was unrelated.

Follow-up (29Jan2018): New information received from investigator included: New event NSTEMI, Investigator initial awareness date.

Follow-up (01Mar2018): New information received from investigator includes: suspect drug details (indication, therapy dates, unit, frequency, and route of administration), medical history (updated information on Diabetes Mellitus II and Hypertension; added ischaemic heart disease, hyperlipidemia, and peripheral arterial disease), reaction data (hospitalization dates), concomitant medications (updated information for bisoprolol, amlodipine, and furosemide; added acetylsalicylic acid and insulin glulisine), and lab data (additional tests).

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the events were related to suspect product Epoetin Zeta. The event pneumonitis was due to intercurrent infection and the subject's relevant history of type 2 diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, ischaemic heart disease and atherosclerosis provided plausible explanations for the event of non-ST evaluated myocardial infarction (NSTEMI).

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-SEP-2017	Basophil count	0.2 %	
2	07-SEP-2017	Basophil count	0.02 x10 3/mm3	0.12 0
3	07-SEP-2017	Blood creatinine	3.30 mg/dl	1 0.50
4	07-SEP-2017	Blood glucose	103 mg/dl	99 60
5	07-SEP-2017	Blood sodium	144 mEq/l	146 134
6	07-SEP-2017	Blood urea	179 mg/dl	50 10
7	26-NOV-2017	Chest scan	pulmonitis	
8	07-SEP-2017	Eosinophil count	3.7 %	

Mfr. Control Number: 2018031606

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
9	07-SEP-2017	Eosinophil count	0.34 x10 3/mm3	0.57 0
10	07-SEP-2017	Glycosylated haemoglobin	7.2 %	5.6 4
11	07-SEP-2017	Glycosylated haemoglobin	55	38 20
12	07-SEP-2017	Haematocrit	37.3 %	45 35
13		Haemoglobin	11.9 g/dl	14.9 12
14	07-SEP-2017	Haemoglobin	11.8 g/dl	14.9 12
15	07-SEP-2017	Lymphocyte count	3.37 x10 3/mm3	3.93 1.50
16	07-SEP-2017	Lymphocyte count	36.8 %	
17	07-SEP-2017	Mean cell haemoglobin	29.6 pg	33 25
18	07-SEP-2017	Mean cell haemoglobin concentration	31.6 g/dl	35 30.5
19	07-SEP-2017	Mean cell volume	93.5	98 80
20	07-SEP-2017	Mean platelet volume	13.1	13.1 9.1
21	07-SEP-2017	Monocyte count	8.4 %	
22	07-SEP-2017	Monocyte count	0.77 x10 3/mm3	0.86 0.14
23	07-SEP-2017	Neutrophil count	50.9 %	
24	07-SEP-2017	Neutrophil count	4.66 x10 3/mm3	8 2
25	07-SEP-2017	Platelet count	231 x10 3/mm3	450 150
26	07-SEP-2017	Red blood cell count	3.99 x10 6/mm3	5.10 3.84
27	07-SEP-2017	Red cell distribution width	14.5 %	16 11
28	07-SEP-2017	White blood cell count	9.16 x10 3/mm3	10 4

13. Relevant Tests

MCV (07Sep2017): 93.5 fL, reference values: 80.0 - 98.0
MPV (07Sep2017): 13.1 fL, reference values: 9.1 - 13.1
HbA1c (07Sep2017): 55 mmol/mol, reference values:20 - 38

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION

Mfr. Control Number: 2018031606

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	4000 IU, cyclic (1 vial every 10 days); Subcutaneous	anemia in kidney failure (Anaemia)	11-AUG-2015 / 20-NOV-2017; 833 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) TAREG (VALSARTAN) ; Unknown

#8) ASPIRIN /00002701/ (ACETYLSALICYLIC ACID) ; Unknown

#9) APIDRA (INSULIN GLULISINE) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Coronary heart disease (Coronary artery disease);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
2016 to Unknown	Relevant Med History	Ischaemic heart disease (Myocardial ischaemia);
Unknown	Relevant Med History from 2006/2007	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Atherosclerosis (Arteriosclerosis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	BULGARIA	13	SEP	1947	70 Years	Male	68.00 kg	17	MAR	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ischemic stroke BLSMA [Ischaemic stroke]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non- interventional study protocol EPOE-09-11 for subject ID BG004095.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 2000 IU, 2x/week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 18-FEB-2016 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DIGOXIN (DIGOXIN) ; 2008 / Ongoing
#2) BISOR (BISOPROLOL FUMARATE) ; 2008 / Ongoing
#3) TRIFAS (TORASEMIDE) ; 2010 / Ongoing
#4) SINTROM (ACENOCOUMAROL) ; 2008 / Ongoing
#5) LODIRIC (ALLOPURINOL) ; 2010 / Ongoing
#6) ROCALTROL (CALCITRIOL) ; 2016 / Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History start date unknown	Chronic pyelonephritis (Pyelonephritis chronic)
Unknown to Ongoing	Relevant Med History start date unknown	Rheumatic heart disease (Rheumatic heart disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018166584

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-MAY-2018

24d. REPORT SOURCE
- ☒ STUDY
- ☐ LITERATURE
- ☒ HEALTH PROFESSIONAL
- ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
- ☒ INITIAL
- ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A contactable physician reported that a 70-year-old Caucasian male subject with unknown ethnicity started to receive epoetin zeta (RETACRIT) subcutaneously at 2000 IU two times weekly from 18Feb2016 and ongoing for renal anemia. Date of first dose reported as 18Feb2016; date of last dose prior to the event reported as 15Mar2018. Dose has not been changed within 3 months prior to the event. The subject had a history of ongoing chronic pyelonephritis and ongoing rheumatic heart failure (RHF); permanent atrial fibrillation (PAF) since 2008 and ongoing; surgery for mesentric thrombosis from 2009 to 2009; gout from an unknown date and ongoing; renal osteodystrophy since 2016 and ongoing, heart failure since 2008 and ongoing, and pre-dialysis. The subject was not exposed to any other erythropoietin - stimulating agents at any time. The subject didn't experience thromboembolic event during treatment with any other ESA. Risk factors reported as chronic atrial fibrillation. Concomitant medications included digoxin orally at 0.125mg once daily since 2008 and ongoing for permanent atrial fibrillation; bisoprolol fumarate (BISOR) orally at 2.5mg once daily since 2008 and ongoing for PAF; torasemide (TRIFAS) orally at 10mg once daily since 2010 and ongoing for heart failure; acetocomarol (SINTROM) orally at 1mg once daily since 2008 and ongoing for PAF; allopuritol (LODIRIC) orally at 100mg once daily since 2010 and ongoing for gout; calcitriol (ROCALTROL) taken for renal osteodystrophy orally from 2016 and ongoing. The subject experienced ischemic stroke BLSMA on 17Mar2018. The patient was admitted to hospital because of the event from 17Mar2018 to 03Apr2018. The event was life threatening. The subject underwent lab tests and procedures which included INR (17Mar2018) 1.67; creatinine (17Mar2018) 152 MKmol/l (normal high: 106 MKmol/l), hematocrit (on an unknown date): 0.31, RBC (on an unknown date): 2.6 T/L, differential count (unknown date) with Lymphocyte (Ly):0.120, Granulocyte (Gr):0.828 and MID:0.052 and Leucocytes:10.8, ECG readings (Unknown date): chronic atrial fibrillation, Cranial CT (unknown date): Old vascular accident in the basal nuclei on the left. Sample data for early ischemic changes in left temporal. On 23Feb2018 with hemoglobin (Hb) 12.0 g/l; on 17Mar2018 with hemoglobin 10.6 g/l(range 14.0-18.0 g/l).
Upon follow-up on 09May2018, it was further reported that "full name of MID reported as - all other cells of differential counting (except for lymphocytes and neutrophils). They are mainly monocytes. On the device go out so MID".
Action taken with suspect drug reported as dose not changed. Outcome of adverse event reported as Recovered/Resolved with Sequel on 03Apr2018. The batch number of epoetin zeta was not available.

The investigator considered that there was not a reasonable possibility that the event ischemic stroke BLSMA was related to the study drug, concomitant medication or to a clinical trial procedure. The reporter believed that the event was not related to the suspect product.

Follow-up (03May2018) New reported information includes: New dosage information, new medical history, lab data, updated recovered date, and clinical course.

Follow-up (09May2018) New reported information includes detailed information for "MID".

Case Comment: Based on the information currently provided, the company concurs with the causality assessment provided by the investigator, considering that there was not a reasonable possibility that the event ischemic stroke BLSMA was related to the study drug, concomitant medication or to a clinical trial procedure. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	17-MAR-2018	Blood creatinine	152	106
2		Computerised tomogram head	ischemic changes	
3		Electrocardiogram	chronic atrial fibrillation	
4		Granulocyte count	0.828	
5		Haematocrit	0.31	
6	23-FEB-2018	Haemoglobin	12.0 g/l	18.0 14.0
7	17-MAR-2018	Haemoglobin	10.6 g/l	18.0 14.0
8	17-MAR-2018	International normalised ratio	1.67	
9		Investigation	0.052	
10		Lymphocyte count	0.120	

Mfr. Control Number: 2018166584

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
11		Red blood cell count	2.6	
12		White blood cell count	10.8	

13. Relevant Tests

creatinine (17Mar2018): 152 MKmol/l.
RBC (unknown date): 2.6 T/L
Cranial CT (unknown date): Old vascular accident in the basal nuclei on the left. Sample data for early ischemic changes in left temporal

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2008 to Ongoing	Relevant Med History	Permanent atrial fibrillation (Atrial fibrillation);
2009 to 2009	Relevant Med History	Surgery (Surgery);
Unknown to Ongoing	Relevant Med History start date unknown	Gout (Gout);
2016 to Ongoing	Relevant Med History	Renal osteodystrophy (Chronic kidney disease-mineral and bone disorder);
2008 to Ongoing	Relevant Med History	Heart failure (Cardiac failure);
Unknown	Relevant Med History	Dialysis (Dialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1933	85 Years	Male	99.00 kg	24	JUL	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

deep leg vein thrombosis left [Deep vein thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study source for Protocol EPOE-09-11, Subject GE-094-0039. This is a Post Authorization Safety Study.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 6000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Nephrogenic anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 15-MAR-2017 / 22-AUG-2018

19. THERAPY DURATION
#1) 526 days

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CLEXANE (ENOXAPARIN SODIUM) ; Ongoing
#2) TARGIN (NALOXONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE) ; Ongoing
#3) MARCUMAR (PHENPROCOUMON) ; Unknown
#4) BISOPROLOL (BISOPROLOL) ; 2017 / Ongoing
#5) CANDESARTAN (CANDESARTAN) ; 2017 / Unknown
#6) PANTOZOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; 2018 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018357453

24c. DATE RECEIVED BY MANUFACTURER
19-DEC-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 85-year-old male subject started to receive epoetin zeta (RETACRIT) subcutaneously from 15Mar2017 to 22Aug2018 at 6000 IU twice weekly for the study indication of nephrogenic anemia. Medical history was significant for atrial fibrillation, hypertension, type 2 diabetes mellitus, prostatic carcinoma, and hydronephrosis since 2017, all ongoing. Concomitant drugs included enoxaparin sodium (CLEXANE) subcutaneously 80 mg daily, naloxone hydrochloride/ oxycodone hydrochloride (TARGIN) 10 mg/5 mg twice a day, bisoprolol 1/2 of the 2.5 mg dose form daily since 2017, pantoprazole sodium sesquihydrate (PANTOZOL) 20 mg daily since 2018, levothyroxine (L-THYROXINE) 150 ug daily since 2018, all ongoing, phenprocoumon (MARCUMAR) currently paused and candesartan 16 mg twice daily since 2017. On 24Jul2018, the subject developed a deep leg vein thrombosis left. The diagnosis "deep vein thrombosis legs" was mentioned in a discharge summary as a secondary diagnosis, because the main reason for admission was shunt obstruction, which was not considered a reportable event, in this subject. Lab tests included hemoglobin (Hgb, normal range 12.6-17.4) on 16Jul2018: 8.4 g/dL (low) and on 22Aug2018: 8.6 g/dL (low). The action taken in response to the event for epoetin zeta was dose reduced to 5000 IU once weekly from 24Aug2018 and ongoing. The subject was treated in hospital. The subject was recovered on 20Aug2018.

The investigator reported that the event had no relationship to administration of epoetin zeta.

Follow-up (22Oct2018): Updates subject data, test details, study drug data, concomitant medication data, and a non-event.

Follow-up (07Nov2018): Provides subject's year of birth and tests.

Follow-up (19Dec2018): New information reported from the investigator includes: patient data (added normal range of Hgb), product data (update stop date of epoetin zeta, updated dosage information for concomitant drugs).

Case Comment: In agreement with the investigator, the Company considers that the reported event deep vein thrombosis legs is possibly unrelated to suspect drug epoetin zeta therapy given no high blood hemoglobin level reported. The ongoing prostatic carcinoma may provide the alternative explanation. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	16-JUL-2018	Haemoglobin	8.4 g/dl	17.4 12.6
2	22-AUG-2018	Haemoglobin	8.6 g/dl	17.4 12.6

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) L-THYROXINE [LEVOTHYROXINE] (LEVOTHYROXINE) ; 2018 / Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Prostatic carcinoma (Prostate cancer);
2017 to Ongoing	Relevant Med History	Hydronephrosis (Hydronephrosis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1935	80 Years	Female	53.00 kg	23	OCT	2015

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
dialysis withdrawal - cardiac arrest [Cardiac arrest]
Infarct on the right brain side [Cerebral infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study, protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 17-JAN-2016
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) *NO SUBJECT DRUG (NO SUBJECT DRUG) Unknown
#2) SILAPO (EPOETIN ZETA)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) no dose given	#1) Unknown
#2) 2000 IU 3x week	#2) Intravenous

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown	#1) Unknown
#2) 15-SEP-2014 / 17-JAN-2016	#2) 490 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) THIAMAZOL (THIAMAZOLE) ; Unknown
#2) AMLODIPIN (AMLODIPINE) ; Unknown
#3) CITALOPRAM (CITALOPRAM) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperthyroidism (Hyperthyroidism)
Unknown to Ongoing	Relevant Med History	Chronic renal insufficiency (Chronic kidney disease)
	stage V with dialysis	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018371605

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-JUN-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2018371605

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A female subject of an unspecified age was enrolled in the study and received no subject drug. Medical history included hyperthyroidism, chronic kidney disease (stage V with dialysis), end-stage renal disease, heart insufficiency, and dementia. Concomitant medication included epoetin zeta (SILAPO) 2000 IU x 3, via intravenous, from 14Mar2015; thiamazole; amlodipine (AMLODIPIN); and citalopram. On 23Oct2015, the subject experienced infarct on the right brain side. The outcome of the event was unknown.

The reporter's assessment of the causal relationship of the event with the suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

Follow-up (16Nov2018): This is follow-up report from a non-interventional study, protocol EPOE-09-11. Chronic kidney disease (stage V), end-stage renal disease, heart insufficiency, and dementia are ongoing, SILAPO was reported under study drug from 15Sep2014 to 17Jan2016 at 2000 IU 3x week. On 23Oct2015, the subject experienced infarction on the right brain side and on 17Jan2016 the patient died. The investigator assessed the causality between the event and study and concomitant medication as unrelated

Follow up (22May2019): New information received from the investigator.
- Year of birth provided, Patient's age at event onset: 80 years.

Follow-up (18Jun2019): This is follow-up report from a non-interventional study, protocol EPOE-09-11.
SILAPO, previously captured as concomitant drug, was now reported as study drug with no changes to the dosage regimen. Indications for the concomitant drugs were provided: thiamazole (THIAMAZOL) was taken for thyroid, amlodipine (AMLODIPIN) for blood pressure and citalopram for depression. Cause of death was provided as dialysis withdrawal. Patient decided to withdrawn from dialysis. The last dialysis was performed on 05Jan2016. Patient died 17Jan2016. New SAE dialysis withdrawal - cardiac arrest with onset date 17Jan2016 and fatal outcome was reported. Action taken for the study drug was reported as withdrawn. According to the investigator, the event was neither related to study medication nor to concomitant medication.

Case Comment: Based on the current available informatoin, the events of Infarct on the right brain side and cardiac arrest with fatal outcome are considered unrelated to the company no subject drug, since there is no company suspected drug given to the patient.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History end-stage renal disease	Renal disease (Nephropathy);
Unknown to Ongoing	Relevant Med History	Heart insufficiency (Cardiac failure);
Unknown to Ongoing	Relevant Med History	Dementia (Dementia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	ITALY	13	FEB	1968	50 Years	Female	59.00 kg	06	APR	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
deep vein thrombosis [Deep vein thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non-Interventional study source for protocol EPOE-09-11, Center ID/Subject ID IT073|0027.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, weekly	#1) Subcutaneous

☐ YES ☐ NO ☒ NA

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 26-JUL-2016 / 03-AUG-2017	#1) 374 days

☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DELTACORTENE (PREDNISONE) ; 18-MAY-2002 / Ongoing
#2) MYFORTIC (MYCOPHENOLATE SODIUM) ; 2007 / Ongoing
#3) ADVAGRAF (TACROLIMUS) ; 18-MAY-2002 / Ongoing
#4) ANTRA [OMEPRAZOLE] (OMEPRAZOLE) ; 18-MAY-2002 / Ongoing
#5) CARVEDILOL (CARVEDILOL) ; 2012 / Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1982 to Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)
1996 to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018413068

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-NOV-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 50-year-old female subject received epoetin zeta (RETACRIT, Solution for injection) from 26Jul2016 to 03Aug2017 at 4000 IU, weekly subcutaneous for renal anaemia. The subject had a relevant history of diabetes mellitus from 1982, ongoing hypertension since 1996, ongoing charcot diasease from 1997, and she was ex-smoker, hyperlipidemia (ongoing), peripheral arterial disease (ongoing), diarrhea. Concomitant medications included mycophenolate sodium (MYFORTIC) since 2007 and ongoing at 360 mg 3x/day orally for kidney transplant and as immunosuppressant, prednisone (DELTACORTENE) 5 mg 1x/day orally for kidney transplant and as immunosuppressant, tacrolimus (ADVAGRAF) orally at 3.5 mg 1x/day for kidney transplant and as immunosuppressant, omeprazole (ANTRA) orally at 40 mg 1x/day for gastritis/ as gastroprotective, all started from 18May2002 and ongoing and carvedilol 50 mg 3x/day as antihypertensive from 2012 and ongoing. On 06Apr2018, 8 months after the withdrawn of Retacrit, the subject experienced a deep vein thrombosis on 06Apr2018, the subject was admitted to hospital because of the event from 06Apr2018 to 10Apr2018. The event assessed as medically significant, hospitalized and not threatening by investigator. Subject's risk factors for thromboembolic events: ex smoker (1 pack daily for 30 years), homocysteinemia (36.97 umol/l, 10Apr2018). The subject underwent ECO Doppler that showed deep vein thrombosis in Apr2018. Lab tests on 09Aug2018 includes: WBC: 5.09 x10^3/uL (range: 4.8-10.8); RBC: 4.88 x10^6/uL (range: 4.0-5.4); HB: 11.00 g/dL (range: 12-16); HCT: 37.30 % (range: 35-48); MCV: 76.40 fL (range: 80-97); MCH: 22.40 pg (range: 25-34); MCHC: 29.40 g/dL (range: 32-38); RDW: 17.00 % (range: 11-16.5); PLT: 108 x10^3/uL (range: 130-400); PCT: 0.11 % ; MPV: 9.90 fL (range: 7.1-10); PDW: 58.70 %; NEUT: 68.4 %; LYMPH: 13.4 %; MONO: 8.6 %; EOS: 7.1 %; BASO: 0.3 %; LUC: 2.20 %; CRP: 0.39 mg/dL (range: 0-0.50). On 09Oct2018: WBC: 4.72 x10^3/uL (range: 4.8-10.8); RBC: 5.00 x10^6/uL (range: 4.0-5.4); HB: 11.40 g/dL (range: 12-16); HCT: 39.50 % (range: 35-48); MCV: 78.90 fL (range: 80-97); MCH: 22.80 pg (range: 25-34); MCHC: 28.80 g/dL (range: 32-38); RDW: 19.00 % (range: 11-16.5); PLT: 154 x10^3/uL (range: 130-400); PCT: 0.17 % ; MPV: 10.70 fL (range: 7.1-10); PDW: 60.30 %; NEUT: 68.9 %; LYMPH: 14.4 %; MONO: 9.7 %; EOS: 5.4 %; BASO: 0.3 %; LUC: 1.40 %. The investigator reported type of dialysis was none, and the subject was at the any time exposed to any other erythropoietin-stimulating agent (ESA). On 30Oct2018, it was reported the subject had been exposed other erythropoietin-stimulating agent (ESA) Aranesp from Feb2018 at 80 mcg weekly (Hemoglobin range: 9.8-11.4), On 06Apr2018, the subject experience deep vein thrombosis during Aranesp treatment (comment: event known on 23Aug2018). The action taken in response to the event for product epoetin zeta was post therapy. The outcome of the event was recovered in May2018.

The investigator considered that the relationship of the event to treatment with Epoetin Zeta, concomitant medications was unrelated. The investigator reported the following: Deep vein thrombosis with hospitalization occurred 8 months after the withdrawn of Retacrit.

Follow-up (29Oct2018): New information reported includes: subject information, suspect drug therapy details and clinical course details.

Follow-up (30Oct2018): New information reported includes: subject information, medical history, event details, concomitant drug details and clinical course details.

Follow-up (21Nov2018): New information reported includes: confirmed the onset date of SAE deep vein thrombosis was 06Apr2018.

Case Comment: In agreement with the investigator, the Company considers that the relationship of the event deep vein thrombosis to treatment with Epoetin Zeta was unrelated given the event occurred 8 months after the withdrawn of Epoetin Zeta. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	10-APR-2018	Blood homocysteine	36.97 umol/l	
2	APR-2018	Echocardiogram	deep vein thrombosis	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
1997 to Ongoing	Relevant Med History	Charcot arthropathy (Neuropathic arthropathy);
Unknown	Relevant Med History 1 pack daily for 30 years	Ex-smoker (Ex-tobacco user);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);
Unknown	Relevant Med History	Diarrhea (Diarrhoea);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	12	JAN	1939	79 Years	Male	85.00 kg	13	OCT	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
thrombosis native arteriovenous fistula [Arteriovenous fistula thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study source and post authorization safety study for protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 3000 UI, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Intravenous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 24-JAN-2017 / 11-FEB-2019

19. THERAPY DURATION
#1) 749 days

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ADIRO (ACETYLSALICYLIC ACID) ; 04-MAY-2018 / Ongoing
#2) LANTUS (INSULIN GLARGINE) ; 2010 / Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypertension (Hypertension)
Unknown	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2018439471

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-AUG-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2018439471

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 79-year-old male subject started to receive epoetin zeta (RETACRIT), via intravenous route of administration, from 24Jan2017 to 11Feb2019 at 3000 UI weekly for renal anaemia. Medical history included hypertension and diabetes mellitus. Concomitant medications included acetylsalicylic acid (ADIRO) (reported as salicylate adiroo 100) via oral from 04May2018 and ongoing for cardiovascular risk high and insulin glargine (LANTUS) (reported as insulina lantus) via subcutaneous from 2010 and ongoing for diabetes mellitus. On 13Oct2018, the subject experienced thrombosis native arteriovenous fistula. Serious criteria reported as an important medical event. ECO-Doppler on 13Oct2018 showed thrombosis native arteriovenous fistula. The subject was treated with enoxaparin sodium (CLEXANE) 40 mcg per day. The last action taken in response to the event for epoetin zeta was dose not changed. The outcome of the event was recovered/resolved with sequel.

The investigator reported there was not a reasonable possibility that the event was related to the study drug or concomitant drug and commented the subject had no significant changes in hemoglobin. Recovery date of the event was not retrievable.

Follow-up (25Oct2018): New information reported includes: Serious event term updated to "thrombosis native arteriovenous fistula" from "thromboembolic event", subject ID and demographic, medical history, lab data, treatment, action taken, and investigator causality.

Follow-up (01Mar2019): New information reported includes: suspect drug retacrit dosage regimen, concomitant medications (adiro and lantus), action taken (amended from NA to dose not changed), rechallenge reportd as unknown (remain NA), and event outcome.

Follow-up (12Jul2019): New information reported includes: product data (route and indication for study drug).

Amendment: This follow-up report is being submitted to amend previously reported information: Additional lab data hemoglobin was added in the field with a result of no significant changes.

Case Comment: Based on the currently available information, the Company considers that the event thrombosis native arteriovenous fistula is unrelated to suspect drug epoetin zeta in accordance with the investigator since the subject had no significant changes in hemoglobin and arteriovenous fistula render the subject more susceptible to thrombosis.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Haemoglobin	No significant changes	
2	13-OCT-2018	Ultrasound Doppler	1.~Thrombosis native arteriovenous fistula	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	08	DEC	1949	69 Years	Male	72.00 kg	16	FEB	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Thrombosis native arteriovenous fistula [Arteriovenous fistula thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study source and post authorization safety study for protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 6000 IU, weekly	#1) Intravenous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 28-SEP-2018 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ZEMPLAR (PARICALCITOL) ; 07-SEP-2016 / Ongoing
#2) MICARDIS (TELMISARTAN) ; 07-SEP-2016 / Ongoing
#3) PREVENCOR [ATORVASTATIN CALCIUM] (ATORVASTATIN CALCI
#4) FUROSEMIDE (FUROSEMIDE) ; 07-SEP-2016 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
07-SEP-2016 to Unknown	Relevant Med History	Hypertension (Hypertension)
07-SEP-2016 to Unknown	Relevant Med History	Hyperlipidaemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019134687

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-OCT-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 69-years-old male subject started to receive intravenous epoetin zeta (RETACRIT, Solution for injection, batch number no retrievable) from 28Sep2018 and ongoing at 6000 IU weekly for renal anaemia. Two independent values of mean doses applied within the period of 3 months prior to the event were: mean dose 1 was at 6000, heamoglobin at 10.1 g/dl; mean dose 2 at 6000, heamoglobin at 9.9 g/dl. There were no any dose changes of study drug within 3 months prior to the event. Medical history included hypertension and hyperlipidaemia, both from 07Sep2016, hyperparathyroidism. Type of dialysis performed for subject was heamodialysis. The subject didn't have the following relevant concurrent and past diseases: ischaemic heart disease, transient ischaemic atiack, peripheral arterial disease, diabetes mellitus, atrial fibrillation, cancer, chronic gastrointestinal disease and diarrhea. The subject wasn't at any time exposed to any other erythropoietin-stimulating agent (esa).The subject didn't have the following risk factors: obesity and smoking; coagulation disorders: factor v leiden, protein c or s deficiency, antithrombin Ill deficiency, prothrombin G20210A mutation, homocysteinemia, recent surgery, trauma, significant and short term weight changes due to fluid retention/excretion, vascular anomalies, aneurysm, immobilisation, recent pregnancy and positive family history. Concomitant medications included paricalcitol (ZEMPLAR) orally from 07Sep2016 and ongoing for hyperparathyroidism, telmisartan (MICARDIS) orally from 07Sep2016 and ongoing for hypertension, atorvastatin calcium (PREVENCOR) orally from 07Sep2016 and ongoing for hyperlipidaemia, furosemide orally from 07Sep2016 and ongoing for hypertension. During remote monitoring the reporter found out that there had been a thrombotic event. Relevant test provided as ECO-DOPPLER on 16Feb2019 showed thrombosis native arteriovenous fistula. Subject experienced thrombosis native arteriovenous fistula on 16Feb2019 which was considered as important medical event. The diagnosis was thrombosis native arteriovenous (AV) fistula. The subject wasn't admitted to hospital because of the event. The event was not threatening. As of 23Apr2019, Trombosis native arteriovenous fistula, not related with RETACRIT use, no significant changes in hemoglobin. The subject underwent relevant lab tests included: haematocrit (normal range: 40.0-54.0) at 32.2%, red blood cell (normal range: 4.50-5.90) at 3.98 x10e6/mm3, red cell distribution width (RDW) (normal range: 11.5-14.5) at 17.3%, lymphocytes (normal range: 20.0-45.0) at 16.5%, absolute monocytes (normal range: 0.3-0.9) at 1.0 x10e3/m, eosinophils (normal range:0.0-5.0) at 5.6%, leucocytes (normal range: 4.0-11.0) at 8.41 x10e3/mm3, mean corpuscular hemoglobin (MCH) (normal range: 27.0-32.0) at 25.9 pg, heamoglobin (normal range: 13.0-17.0) at 10.3 g/dl, duplex and doppler sonography showing thrombosis native A-V fistula and differential blood count. Blood test-General biochemistry included: Glucose: 80 mg/dl (normal range 82-115), Urea: 144 mg/dl (normal range 16-50), Creatinine: 7.37 mg/dl (normal range 0.70-1.20), Potassium: 6.1 mEq/l (normal range 3.5-5.1), Phosphorus: 5.1 mg/dl (normal range 2.5-4.5), Iron: 30 ug/dl (normal range 33-193). Proteinogram included: Albumin: 53.8 % (normal range 55.8-66.1), Gamma: 21.7 % (normal range 11.1-18.0) and 1.7 g/dl (normal range 0.7-1.5). Date of awareness 25Mar2019. Last action taken in response to the event for Epoetin Zeta was reported as dose not changed. No treatment prescribed. The outcome of the event was recovered/resolved with Sequel. Recovery date of the event was not retrievable. Sequelae meant that trombo did not disappear from inside the vein. It was also reported that thrombosis native arteriovenous fistula was ongoing.

The investigator considered there was not a reasonable possibility that the event thrombosis native arteriovenous fistula was related to the study medication Epoetin Zeta and concomitant drugs.

Follow-up (23Apr2019): New information reported from the investigator includes: medical history (Hyperparathyroidism), event information.

Follow-up (16Jul2019): New information reported includes: study drug details (indication, route and dose history), start date of medical history (hypertension and hyperlipidaemia), additional medical history details, concomitant drugs details (dose and frequency), additional relevant lab tests and clinical course.

Follow-up (09Aug2019): New information reported includes: relevant lab tests.

Lot/batch number of epoetin zeta has been requested.

Follow-up (30Oct2019): New information included: subject date of birth and age updated, batch number no retrievable.

Case Comment: In agreement with the investigator, the company considered that there was not a reasonable possibility that the reported event Thrombosis arteriovenous fistula was related to study medication Epoetin Zeta. The event is most likely related to an intercurrent or underlying condition. The follow up information received does not alter the previous company evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood albumin	53.8 %	66.1 55.8
2		Blood creatinine	7.37 mg/dl	1.20 0.70
3		Blood glucose	80 mg/dl	115 82
4		Blood iron	30	193 33

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
5		Blood phosphorus	5.1 mg/dl	4.5 2.5
6		Blood potassium	6.1 mEq/l	5.1 3.5
7		Blood urea	144 mg/dl	50 16
8		Differential white blood cell count		
9		Eosinophil count	5.6 %	5.0 0.0
10		Haematocrit	32.2 %	54.0 40.0
11		Haemoglobin	10.3 g/dl	17.0 13.0
12		Haemoglobin	No significant changes	
13		Haemoglobin	9.9 g/dl	
14		Haemoglobin	10.1 g/dl	
15		Immunoglobulins	1.7 g/dl	1.5 0.7
16		Immunoglobulins	21.7 %	18.0 11.1
17		Lymphocyte count	16.5 %	45.0 20.0
18		Mean cell haemoglobin	25.9 pg	32.0 27.0
19		Monocyte count	1.0	0.9 0.3
20		Red blood cell count	3.98 x10 6/mm3	5.90 4.50
21		Red cell distribution width	17.3 %	14.5 11.5
22		Ultrasound Doppler	Thrombosis native arteriovenous fistula	
23	16-FEB-2019	Ultrasound Doppler	Thrombosis native arteriovenous fistula	
24		White blood cell count	8.41 x10 3/mm3	11.0 4.0

13. Relevant Tests

Absolute monocytes (unknown date): 1.0 x 10e3/m (normal range: 0.3-0.9)
Iron (unknown date): 30 ug/dl (normal range 33-193)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#3) PREVENCOR [ATORVASTATIN CALCIUM] (ATORVASTATIN CALCIUM) ; 07-SEP-2016 / Ongoing

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hyperparathyroidism (Hyperparathyroidism);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
UNKNOWN	SPAIN	06	AUG	1928	88 Years	Female	Unk	10	FEB	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Thrombosis pulmonar bilateral [Pulmonary thrombosis]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Non-Interventional Study report from the ovservational study EPOE-09-11. A Physician reported that an 88-year-old female subject started to receive epoetin zeta (RETACRIT, Solution for injection).

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 1000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) secondary anemia to chronic kidney disease (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 25-JUL-2016 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ATROVENT (IPRATROPIUM BROMIDE) ; Unknown
#2) FUROSEMIDA [FUROSEMIDE] (FUROSEMIDE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Bronchitis (Bronchitis)
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019143892

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-MAY-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

On 25Jul2016, the subject received first dose of Retacrit at 1000 IU weekly via subcutaneous for secondary anemia to chronic kidney disease. The subject relevant histories: bronchitis, ongoing hyperlipidemia, transient ischaemic attack and ongoing hypertension. The subject did not have below risk factors (obesity, smoking, significant and short term weight changes due to fluid retention /excretion, vascular anomalies, immobilization, recent pregnancy). Concomitant medications included ipratropium bromide (ATROVENT) orally for bronchitis, furosemide (FUROSEMIDA [FUROSEMIDE]) orally for hypertension. On 10Feb2017 the subject experienced thrombosis pulmonar bilateral. Verbatim: Sudden dispnea no thoratic pain, with suspect of thrombosis, pulmonar gammagraphic was done and the result was positive for thrombosis. The seriousness criteria for this event was hospitalization and life-threatening. The subject was hospitalized from 10Feb2017 to 20Feb2017. The subject underwent lab tests which included pulmonar gammagraphic (thrombosis bilateral) on 10Feb2019; on 13Feb2017: Neutrophils (91.6 %, 10.35 x10 3/mm3), Lymphocytes (6.6%, 0.75 x10 3/mm3), monocytes (1.6%, 0.18 x10 3/mm3), ESR: 120.00mm (range 0-15), urea 234 mg/dl, Uric acid 12.2 mg/dl, creatinine 2.16 mg/dl, Atherogenic index: 4.76 mlg/100, Phosphorus 5.71 mg/dl, amylase 132 IU/L; on 16Feb2017: Lung perfusion scan: Perfusion defects are observed in the lingula and anterior segment of the upper lobe of the left lung and in all the segments of the upper lobe of the right lung; Pulmonary ventilation scan: Homogeneous uptake of the radiopharmaceutical is observed in both lungs. In both studies, an elevation of the right lung is visualized. CONCLUSION: Perfusion defects in both lungs, not concordant with the ventilation study and compatible with bilateral pulmonary thromboembolism. The therapy was in progress at the time of the event. The investigator also confirmed that the answer was correct as NA, that the treatment has not been suspended. The female subject was admitted due to progressive dyspnea at rest of one week of evolution, with greenish expectoration, which did not improve after antibiotic and steroid treatment. On 10Feb2019: eosinophils (0%, 0 x10 3/mm3), red blood cells (3.68 x10 6/mm3), MCHC (32.3 g/dl), Platelets (364 x10 3/mm3), plateletcrit (0.4 %). Chest Rx: Vascular and fluid redistribution in fissures. Pulmonary scintigraphy: bilateral PET. The action taken in response to the event for product retacrit was dose was not changed. The subject received Sintrom (daily) from 10Feb2017 as treatment for thrombosis. Treatment with LMWH and subsequent oral anticoagulation were started. Home discharge 10 days after admission with good clinical evolution. The outcome of the event at the time of the report was recovered with sequel on 20Feb2017. The investigator considered that the relationship of the event to treatment with Retacrit was unrelated.

Amendment: This follow-up report is being submitted to amend previously reported information: update study information.

Follow-up (22May2019): New information reported from the same contactable physician includes: drug information including start date, route and dosage regimen; medical history; event details including seriousness criteria, hospitalization details, outcome, lab data and treatment.

Follow-up (18May2020): New information received from the investigator confirmed: product details and dosage, indication, event details, lab data and treatment.

Case Comment: Based on the available information, there is not a reasonable possibility that the reported event Thrombosis pulmonary bilateral is related to the study drug epoetin zeta (RETACRIT), in this 88-year-old female subject. The event is more likely an intercurrent condition. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	13-FEB-2017	Amylase	132 IU/l	100 20
2	13-FEB-2017	Amylase	132 IU/l	
3	13-FEB-2017	Blood creatinine	2.16 mg/dl	0.9 0.5
4	13-FEB-2017	Blood phosphorus	5.71 mg/dl	4.5 2.7
5	13-FEB-2017	Blood urea	234 mg/dl	20 10
6	13-FEB-2017	Blood uric acid	12.2 mg/dl	5.7 2.4
7		Chest X-ray Vascular and fluid redistribution in fissures	Vascular and fluid redistribution	
8	10-FEB-2019	Eosinophil count	0 x10 3/mm3	0.50 0
9	10-FEB-2019	Eosinophil count	0 %	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
10		Investigation	Perfusion defects in both lungs...	
		Perfusion defects in both lungs, not concordant with the ventilation study and compatible with bilateral pulmonary thromboembolism		
11	13-FEB-2017	Investigation	4.76 mlg/100	
12	13-FEB-2017	Lymphocyte count	6.6 %	
13	13-FEB-2017	Lymphocyte count	0.75 x10 3/mm3	4.10 1.40
14	10-FEB-2019	Mean cell haemoglobin concentration	32.3 g/dl	35 32.6
15	13-FEB-2017	Monocyte count	1.6 %	
16	13-FEB-2017	Monocyte count	0.18 x10 3/mm3	0.90 0.30
17	13-FEB-2017	Neutrophil count	10.35 x10 3/mm3	7.50 2.20
18	13-FEB-2017	Neutrophil count	91.6 %	
19	10-FEB-2019	Platelet count	364 x10 3/mm3	363 159
20	10-FEB-2019	Plateletcrit	0.4 %	0.3 0.2
21	10-FEB-2019	Red blood cell count	3.68 x10 6/mm3	5.10 3.80
22	13-FEB-2017	Red blood cell sedimentation rate 120.00mm (range 0-15)	120.00 mm	15 0
23		Ventilation/perfusion scan	bilateral PET	
24	16-FEB-2017	Ventilation/perfusion scan	Perfusion defects in both lungs	
		Perfusion defects are observed in the lingula and anterior segment of the upper lobe of the left lung and in all the segments of the upper lobe of the right lung.		
25	16-FEB-2017	Ventilation/perfusion scan	Homogeneous uptake of the radiopharmaceutical	
		Homogeneous uptake of the radiopharmaceutical is observed in both lungs. In both studies, an elevation of the right lung is visualized.		
26	10-FEB-2019	Ventilation/perfusion scan	thrombosis bilateral	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Transient ischaemic attack (Transient ischaemic attack);
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	08	NOV	1931	85 Years	Female	Unk		FEB	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Acute myocardial infarction [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANEMIA (PASCO II)

This is a Non-Interventional Study from the observational study EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 3000 IU, monthly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) JUL-2016 / 24-JUL-2017

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CARDURAN (DOXAZOSIN MESILATE) Tablet ; Ongoing
#2) SEGURIL (FUROSEMIDE) Tablet ; Ongoing
#3) ALIPZA (PITAVASTATIN CALCIUM) Tablet ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)
2003 to Ongoing	Relevant Med History	Renal disease (Nephropathy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019143957

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-MAY-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An 85-year-old female subject started to receive epoetin zeta (RETACRIT) via subcutaneous at 3000 IU monthly from Jul2016 to 24Jul2017 for anemia. Ongoing subject history included hypertension, kidney renal disease since 2003, haemodialysis, hyperlipidemia and cholesterolemia (unspecified). Ongoing concomitant drugs included doxazosin mesilate (CARDURAN) orally for hypertension arterial, furosemide (SEGURIL) orally for hypertension arterial and pitavastatin calcium (ALIPZA) orally for cholesterolemia. The adverse event term was reported as acute myocardial infarction in Feb2017. The event was considered serious. Investigator awareness date was reported as Mar2017. The seriousness criteria was reported as life-threatening and hospitalization/prolongation of hospitalization. The subject suffered the acute myocardial infarction at home and was hospitalized in other hospital. The last dose prior to the event was used in Jan2017. The subject did not expose to any other erythropoietin-stimulating agent (ESA). And the subject did not have other risk factors (eg. obesity, smoking, coagulation disorders, recent surgery, trauma, vascular anomalies, aneurysm, ischaemic heart disease, transient ischaemic attack, peripheral arterial disease, diabetes mellitus, atrial fibrillation, cancer, chronic gastrointestinal disease, diarrhea and etc.) or positive family history. Laboratory/Diagnostic results included haemoglobin values: 30Aug2016 HB 11.8 g/dl (11.4-15.5); 31Oct2016 HB 12.5 g/dl (11.4-15.5); 16Jan2017 HB 11.4 g/dl (11.4-15.5); 01Mar2017 HB 10.7 g/dl (11.4-15.5); 16Jun2017 HB 10.9 g/dl (11.4-15.5); and 09Oct2017 HB 10.7 g/dl (11.4-15.5). The action taken for epoetin zeta was unknown in spite that the drug stop date was provided. The event outcome was recovered in Feb2017. The investigator considered there was not a reasonable possibility that the event acute myocardial infarction was related to the study drug or to a concomitant drug.

The information on the lot/batch number has been requested.

Amendment: This follow-up report is being submitted to amend previously reported information: updated study information.

Follow-up (13May2019): New information received from the investigator includes: patient information (gender and age), medical history, concomitant medications, serious adverse event description with seriousness criteria and reporter comment on causal relationship.

The information on the lot/batch number has been requested.

Follow-up (22May2020): New information received from the investigator via the Clinical Team, providing the lab data results.

Case Comment: Based on the available information and on the compatibility with the drug's known safety profile, the company (Pfizer) considers that a causal relationship between the reported event myocardial infarction and suspect drug epoetin zeta cannot be excluded. Patient's history of hypertension arterial and hypercholesterolemia may have played a contributory role.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-AUG-2016	Red blood cell count	11.8 g/dl	15.5 11.4
2	31-OCT-2016	Red blood cell count	12.5 g/dl	15.5 11.4
3	16-JAN-2017	Red blood cell count	11.4 g/dl	15.5 11.4
4	01-MAR-2017	Red blood cell count	10.7 g/dl	15.5 11.4
5	16-JUN-2017	Red blood cell count	10.9 g/dl	15.5 11.4
6	09-OCT-2017	Red blood cell count	10.7 g/dl	15.5 11.4

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypercholesterolemia (Hypercholesterolaemia);
Unknown to Ongoing	Relevant Med History	Haemodialysis (Haemodialysis);
Unknown to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1937	81 Years	Male	67.00 kg	24	FEB	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study source and post authorization safety study for Protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 4000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 29-JUN-2016 / Ongoing

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SIMVASTATIN (SIMVASTATIN) ; 2016 / Ongoing
#2) FUROSEMID (FUROSEMIDE) ; 2016 / Ongoing
#3) AMLODIPINE (AMLODIPINE) ; 2016 / Ongoing
#4) CANDESARTAN (CANDESARTAN) ; 2016 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Renal anaemia (Nephrogenic anaemia)
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019145681

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-JUN-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2019145681

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

An approximately 81-year-old male subject started to receive epoetin zeta (EPOETIN ZETA, Solution for injection). On 29Jun2016 the subject received first dose of Epoetin Zeta at 4000 IU, 2x/week via an unspecified route of administration for renal anaemia. The subject had a relevant history of renal anaemia, diabetes mellitus and hypertension from unknown date and ongoing, CKD from 2016 and ongoing. Concomitant medications included simvastatin orally, furosemide (FUROSEMID) orally, amlodipine orally, candesartan orally. On 24Feb2019 the subject experienced non-ST segment elevation myocardial infarction (NSTEMI). As described: subject was admitted to hospital due to respiratory insufficiency and dyspnea. NSTEMI was diagnosed but patient refused invasive therapy, event was treated with medication (ASS, BRILIQUE). The seriousness criteria for this event were hospitalization. The product Epoetin Zeta dose was not changed as a result of event. The outcome of the event at the time of the report was: recovered on 30Mar2019. The subject was hospitalized on an unknown date. On an unknown date, the subject was discharged from the hospital. The investigator considered that the relationship of the event to treatment with Epoetin Zeta was unrelated, not provided regarding concomitant medication.

Follow-up (11Apr2019): New information received from the investigator includes: completion of DCA: last dose of epoetin zeta prior to event was on 22Feb2019, route of administration: subcutaneous, dose had not been changed during the last three month prior to event. A lot number was not available. The patient took no other erythropoietin stimulating agents. Lab values for haemoglobin were provided for 07Jan2019 (11.6) and 18Feb2019 (8.5) - it was confirmed, that no other lab values or examination results were available. Additional Relevant Medical History was reported as: cardiac ischaemia, ongoing, stroke in 2014, haemodialysis, start date for hypertension reported as 2014. The patient had no other Medical History or Risk Factors.

Follow-up (24Jun2019): New information reported includes: The age at the onset of event was 81 years. The subject was admitted on 24Feb2019 and discharged on 30Mar2019. The investigator considered the event was unrelated to concomitant medication.

Case Comment: Based on the available information and in agreement with investigator, the Company considers the reported event NSTEMI is unrelated to suspect drug epoetin zeta but more likely inter-current illness in this 82-years-old male with medical history of diabetes mellitus and hypertension.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-JAN-2019	Haemoglobin	11.6 g/dl	
2	18-FEB-2019	Haemoglobin	8.5 g/dl	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2014 to Ongoing	Relevant Med History	Hypertension (Hypertension);
2016 to Ongoing	Relevant Med History	Chronic kidney disease (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History	Cardiac ischaemia (Myocardial ischaemia);
2014 to 2014	Relevant Med History	Stroke (Cerebrovascular accident);
Unknown	Relevant Med History	Haemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1932	84 Years	Female	97.70 kg	07	OCT	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
thromboembolic event [Embolism]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Non-Interventional Study report from the observational study EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 2000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) OCT-2015 / Ongoing

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure)
Unknown	Relevant Med History D638g	Renal anaemia (Nephrogenic anaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019193578

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-MAY-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A Physician and a other HCP reported that an 84-year-old (approximate age) female subject started to receive epoetin Zeta (RETACRIT), solution for injection in Oct2015 and ongoing at 2000 IU weekly for the treatment of renal anemia. The subject had a relevant history of renal failure. On 07Oct2016, the subject was hospitalized due to [illegible], obstruction was detected in hospital by chance. The event was assessed as non-serious. The subject underwent lab tests and procedures which included plethysmography with result as obstruction. The product epoetin Zeta dose was not changed as a result of event. The outcome of the event at the time of the report was recovered on 11Oct2016. The causality assessment was not provided.

Follow-up (09May2019): This is a follow-up report received from the investigator.

The subject was hospitalized due to fall. Obstruction was detected in hospital by chance. The causality assessment for event was "No causality". Seriousness of event was confirmed as "not serious". Lot number and expiration date of epoetin Zeta were not available.

Follow-up (13Sep2019): New information received from the investigator includes: medical history besides the renal failure were renal anaemia (D638G); adipositas BMI 35 (E6601G); Hypothyreose/ Thyreoiditis (E038G); diabetic nephropaty (E1120G); COPD (J4489G), hypertension (J1000G). The event obstruction was a moderate obstruction of the lungs.

Follow-up (25May2020): New information received from the investigator includes: Event term confirmed to be changed to thromboembolic event. Case upgraded to serious.

Case Comment: Based on the available information and on the compatibility with the drug's known safety profile, the company (Pfizer) considers that a causal relationship between the "thromboembolic event" and suspect drug epoetin zeta (RETACRIT) cannot be excluded.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-OCT-2016	Plethysmography	obstruction	

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History BMI 35 (E6601G)	Adipositas (Obesity);
Unknown	Relevant Med History E038G	Hypothyreosis (Hypothyroidism);
Unknown	Relevant Med History E1120G	Nephropathy (Nephropathy);
Unknown	Relevant Med History J4489G	COPD (Chronic obstructive pulmonary disease);
Unknown	Relevant Med History J1000G	Hypertension (Hypertension);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		SEP	1976	41 Years	Female	104.70 kg	19	NOV	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Non-Interventional Study report and post authorization safety study for Protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 3000 IE, once a week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 16-JAN-2017 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) BISOPROLOL (BISOPROLOL) ; Unknown
#2) EBRANTIL [URAPIDIL] (URAPIDIL) ; Unknown
#3) APIDRA (INSULIN GLULISINE) ; Unknown
#4) KREON 25000 (PANCREATIN) ; Unknown
#5) ASS (ACETYLSALICYLIC ACID) ; Unknown
#6) EFIENT (PRASUGREL HYDROCHLORIDE) ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
31-AUG-2016 to Ongoing	Relevant Med History	Hypertension (Hypertension)
31-AUG-2016 to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019210839

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-SEP-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 41-year-old female subject started to receive epoetin zeta (RETACRIT), subcutaneously from 16Jan2017 and ongoing at 3000 IE, once a week for renal anemia. The subject's medical history included diabetes mellitus from 31Aug2016 and ongoing and hypertension from 31Aug2016 and ongoing, risk factor (for thromboembolic events) included adipositas (BMI = 41.9). The subject's concomitant medications included Bisoprolol 10 mg at 5 mg, twice a day (0.5-0-0.5), Ebrantil 30 mg at 30 mg, three times a day (1-1-1), Apidra via insulin pump, Kreon 25000 at 25000, twice a day (1-0-1), ASS 100 at 100, once a day (0-1-0), Efient 10 mg at 10 mg, once a day (1-0-0), Amlodipin 5 mg at 5 mg, twice a day (1-0-1), Valsartan 160 mg at 160 mg, once a day (1-0-0), Atorvastatin 80 mg at 80 mg, once a day (1-0-0). The subject experienced Non ST segment elevation myocardial infarction (NSTEMI) on 19Nov2017: Ramus circumflexus (RCX) stenosis on an unspecified date. The serious criteria reported as hospitalization and life threatening. The subject underwent lab tests which included coronary angiography: stenosis on unknown date, Electrocardiogram (EKG): regular rhythm on 19Nov2017, blood test showed troponin T (high) on 19Nov2017, Hb 5.39 mmol/ l on 05Feb2018, Hk 26% on 05Feb2018, erythrocytes 2.93 Tpl on 05Feb2018, leukocytes 5.78 Gptl on 05Feb2018, and BMI was 41.9 on unspecified date. As of 30Aug2019, it was reported investigator's awareness date was unknown, the subject had not died. kind of dialysis was none (pre-dialysis). Subject was not receive other erythropoietin-stimulating agents at any time. The action taken in response to the event for epoetin zeta was dose not changed. The outcome of event was recovered on 27Nov2017. An autopsy was not performed for the subject (as reported).

Causality has been assessed as unrelated to study drug and concomitant medication by the investigator.

Follow-up (10Jul2019): New information reported includes: subject details.

Follow up (30Aug2019): New information received from investigator includes: indication, clinical details.

Follow-up (20Sep2019): New information received from the investigator included: medical history, risk factor, concomitant medications and lab results.

Case Comment: Based on the information currently provided, the company concurs with the causality assessment provided by the investigator, considering the event as unrelated to study drug and concomitant medication. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Angiocardiogram	stenosis	
2	19-NOV-2017	Blood test	Troponin T (high)	
3		Body mass index	41.9	
4	19-NOV-2017	Electrocardiogram	Regular rhythm	
5	05-FEB-2018	Haematocrit	26 %	
6	05-FEB-2018	Haemoglobin	5.39 mmol/l	
7	05-FEB-2018	Red blood cell count	2.93 Tpl	
8	05-FEB-2018	White blood cell count	5.78 Gptl	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) AMLODIPINE (AMLODIPINE) ; Unknown

#8) VALSARTAN (VALSARTAN) ; Unknown

#9) ATORVASTATIN (ATORVASTATIN) ; Unknown

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History BMI 41.9	Adipositas (Obesity);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1933	83 Years	Male	80.50 kg	08	APR	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Non STEMI [Acute myocardial infarction]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Non-Interventional Study report from the observational study EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 1x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 24-FEB-2016 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
24-OCT-2011 to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)
20-OCT-2014 to Ongoing	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019210884

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-APR-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 83-year-old male started to receive epoetin zeta (RETACRIT), subcutaneous from 24Feb2016 once a week; from 18Jan2017 (dose changes in the last 3 months before the event occurred) and ongoing, at dose 4000 IU, 3 times a week for renal anemia. Medical history included ongoing hyperlipidemia from 11Jul2016, ongoing diabetes mellitus form 24Oct2011, ongoing hypertension from 20Oct2014, and aortic valve stenosis. The subject's concomitant medications were not reported. The subject experienced Non STEMI on 08Apr2017. Seriousness criteria reported as hospitalization and life threatening. The subject underwent lab tests which included blood tests: high Troponin T on 08Apr2017 and ECG (electrocardiogram): no objections on 08Apr2017. As of 30Aug2019, confirmation of Hb level (Hb (18Apr2017): 5.31 mmol/l; Hb (24Apr2017): 5.81 mmol/l; Hb (22Mar2017): 6.52 mmol/l)). Type of dialysis (hemodialysis), Hb level before the dose change: 6.27 mmol/l, Hb level after the dose change: 6.52 mmol/l. Lab values from the last 3 months (Hemoglobin (unknown date): 4.6; Hematocrit (unknown date): 0.23; CRP (unknown date): 34.1; ECG (08Apr2017): provided; Troponin T (unknown date): 675; D-Dimer (unknown date): 2282; Roentgen Thorax (08Apr2017, 09Apr2017, 12Apr2017): present; Sono pleura (10Apr2017): present.). The patient received no other erythropoietin stimulating factors. The patient did not have any risk factors which could prone the thromboembolic events. The action taken in response to the event for epoetin zeta was dose not changed. The outcome of event was recovered on 12Apr2017. Causality between the event and the study drug epoetin zeta (RETACRIT) was assessed as unrelated by the investigator.

Follow-up (30Aug2019): New information received from the investigator included: lab data, indication, dose regimen, medical history, clinical details.

Follow-up (30Apr2020): New information received from the investigator included: date of birth update. The patient was 83 years old at the time of event onset.

Case Comment: In agreement with the Investigator, the event Non STEMI is most likely related to intercurrent or underlying conditions and unrelated to suspect product EPOETIN ZETA. The subject's medical history of diabetes mellitus, hypertension and aortic valve stenosis may provide an alternative explanation..

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-APR-2017	Blood test	High Troponin T	
2	2017	C-reactive protein	34.1	
3	08-APR-2017	Chest scan	present	
4	09-APR-2017	Chest scan	present	
5	12-APR-2017	Chest scan	present	
6	08-APR-2017	Electrocardiogram	no objections	
7	2017	Fibrin D dimer	2282	
8	2017	Haematocrit	0.23	
9	22-MAR-2017	Haemoglobin	6.52 mmol/L	
10	18-APR-2017	Haemoglobin	5.31 mmol/L	
11	24-APR-2017	Haemoglobin	5.81 mmol/L	
12	2017	Haemoglobin	4.6 mmol/L	
13	2017	Troponin T	675	
14	10-APR-2017	Ultrasound scan	present	

Mfr. Control Number: 2019210884

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	4000 IU, 3x/ week; Subcutaneous	renal anemia (Nephrogenic anaemia)	18-JAN-2017 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Aortic valve stenosis (Aortic valve stenosis);
11-JUL-2016 to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		JUN	1949	70 Years	Female	81.00 kg	18	JUL	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

peripheral arterial disease [Peripheral arterial occlusive disease]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a non-interventional study for Protocol EPOE-09-11. This 70-year-old female subject started to receive treatment with epoetin zeta (RETACRIT) 4000 IU weekly, subcutaneously, on 12Oct2016, for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, weekly	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-OCT-2016 / Ongoing	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) HUMALOG (INSULIN LISPRO) ; Ongoing
#2) ALFACALCIDOL (ALFACALCIDOL) ; Ongoing
#3) ASS (ACETYLSALICYLIC ACID) ; Ongoing
#4) SIMVA ARISTO (SIMVASTATIN) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)
Unknown to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019328714

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
16-AUG-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

renal anemia. The last dose prior to the event was administered on 12Jul2019. The subject's medical history included hypertension and diabetes mellitus type II, both from unspecified date and ongoing. On follow-up, it was reported that patient's dialysis hemodialysis. Additional information provided: The dose had not been changed within the last three months prior to the event; the subject did not receive other erythropoietin-stimulating agents at any time; and there were no risk factors for thromboembolic events or other risk factors reported. Her concomitant medications included insulin lispro (HUMALOG) for diabetes, alfacalcidol as prophylaxis, acetylsalicylic acid (ASS) for hypertension, and simvastatin (SIMVA ARISTO) as prophylaxis, all ongoing. On 18Jul2019, the subject experienced peripheral arterial disease which required hospitalization. The clinical course was as follows: subject was admitted to hospital on 18Jul2019 with diagnosis of peripheral arterial disease. Thromboendarterectomy of arteria (a.) femoralis communis plus a. iliaca externa was conducted on 19Jul2019. Test data included: hemoglobin 14.8 g/dl on 13May2019; and on 08Jul2019, blood alkaline phosphatase (AP): 120 IU/l (range: 35-104), blood creatinine: 5.13 mg/dl (range: 0.50-1.10), PTH intact (blood parathyroid hormone): 188 pg/ml (range: 15-65), blood phosphorus: 7.5 mg/dl (range: 2.5-4.5), urea: 113 mg/dl (range: 15.0-46.0), Kt/V according to Daugirdas (dialysis efficacy test): 2.75 (no units or reference range provided); hemoglobin: 14.6 g/dl, and erythrocytes: 5.06 x10 6/mm3 (range: 4.20-5.40). It was added that the two main dose values that were within the last three months prior to the event: main dose 1: 08Jul2019 4000 IU/week, Hb 14.6 g/dl, main dose 2: 13May2019 4000 IU/week, Hb 14.8 g/dl. There was action taken with the study drug in response to the event. The subject recovered from the event on 24Jul2019. As per hospital discharge letter dated 23Jul2019, the subject was under inpatient therapy from 18Jul2019 to 24Jul2019. The diagnoses was: peripheral artery occlusive disease St. 22b on the left, dialysis-dependent renal insufficiency, diabetes mellitus type II, art. hypertension, anemia, state after Cimino shunt placement on the right, 40% stenosis of A. carotis interna bilateral. Therapy included: Thrombo-endarterectomy of A. femoralis communis, retrograde thrombo-endarterectomyof A. iliaca externa, ligature of A. femoralis superficialis and patch plastic surgery of A. femoralis communis and of A. femoris profunda on the left and intraoperative angiography as well as angioplasty with stent implantation in the left A. iliaca communis and A. iliaca externa on 19Jul2019. Therapy recommendation: We ask for regular checks of wounds and findings as well as regular change of dressing. Removal of inserted clip material should take place from postoperative day 12 - 14. The intake of a thrombocyte aggregation inhibitor (e. g. ASS) as well as a statin is induced life-long. At the time of discharge wound healing was properly and per primam. Ergometric exercises in the area of groin (e. g. going by bike) should be relinquished for approximately three months. Last medications: Alfacalcidol 0.5 mg 1-0-0, ASS 100 1-0-0, Simvastatin 10 0-0-1, Pantoprazol 20 1-0-0, Humalog 25-0-15. The investigator reported there was not a reasonable possibility that the event was related to the study drug or to any concomitant medication.

Follow-up (16Aug2019): Updates subject data (ethnicity), study drug data, type of dialysis, test data, treatment data, and hospital discharge summary.

Case Comment: Based on information provided, the company concurs with investigator that the event peripheral arterial disease is an intercurrent condition, thus unrelated to the suspect drug epoetin zeta. The follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-JUL-2019	Blood alkaline phosphatase	120 IU/l	104 35
2	08-JUL-2019	Blood creatinine	5.13 mg/dl	1.10 0.50
3	08-JUL-2019	Blood parathyroid hormone	188	65 15
4	08-JUL-2019	Blood phosphorus	7.5 mg/dl	4.5 2.5
5	08-JUL-2019	Blood urea	113 mg/dl	46.0 15.0
6	08-JUL-2019	Dialysis efficacy test	2.75	
7	13-MAY-2019	Haemoglobin	14.8 g/dl	
8	08-JUL-2019	Haemoglobin	14.6 g/dl	
9	08-JUL-2019	Red blood cell count	5.06 x10 6/mm3	5.40 4.20

ADDITIONAL INFORMATION

13. Relevant Tests

PTH intact (08Jul2019): 188 pg/ml

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	03	MAR	1941	78 Years	Male	94.50 kg	04	MAY	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

NSTEMI [Acute myocardial infarction]
cardiac failure [Cardiac failure]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-interventional study source and post authorization safety study for Protocol EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1) 4000 IU, 2x/week

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) 08-JUN-2016 / Ongoing

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NOVOMIX 30 Flexpen (INSULIN ASPART, INSULIN ASPART PROT
#2) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; 14-MAR-2014 / Ongoing
#3) EZETIMIBE SANDOZ (EZETIMIBE) Tablet ; 24-APR-2015 / Ongoing
#4) ALVEDON (PARACETAMOL) Film-coated tablet ; 19-JAN-2019 / Ongoing
#5) ETALPHA (ALFACALCIDOL) Capsule, soft ; 09-NOV-2018 / Ongoing
#6) EXTRANEAL (CALCIUM CHLORIDE DIHYDRATE, ICODEXTRIN, M

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
1995 to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus)
OCT-2016 to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
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Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2019431417

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-DEC-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The subject received peritoneal dialysis. This 78-year-old male subject started to receive treatment with epoetin zeta (RETACRIT) via subcutaneous at 4000 units twice weekly from 08Jun2016 and ongoing for renal anemia, date of last dose before the event was 30Apr2019. Mean dose 1: 8000 units/week 18Mar2019, haemoglobin 110 g/l. Mean dose 2: 8000 units per week, haemoglobin 118 g/l 05Feb2019. There were no changes in the dose of epoetin zeta within 3 months prior to the event. The subject was not at any time exposed to any other erythropoetin-stimulating agent. Risk factors for thromboembolic events were reported as No for obesity, smoking, recent surgery, trauma, significant and short-time weight changes due to fluid retention/excretion, vascular anomalies, aneurysm, immobilisation, recent pregnancy and positive family history. Risk factors were reported as unknown for Factor V Leiden, Protein C or S deficiency, antithrombin III deficiency, prothrombin G20210A mutation and homocysteinemia. The subject did not have transient ischemic attack, peripheral arterial disease, atrial fibrillation, cancer, chronic gastrointestinal disease or diarrhoea. Ongoing medical history included diabetes type 2 from 1995, chronic renal failure and peritoneal dialysis from Oct2016, atrioventricular block from 19Jan2019 (treated with pacemaker), hypertension from 1990 (also reported from approximately 1995), spinal stenosis from 23Mar2018, hyperlipidemia from 27Apr2010, and ischeamic heart disease from 04May2019 and ongoing, diagnosed at hospitalization. Concomitant medications included insulin aspart, insulin aspart protamine (crystalline) (NOVOMIX 30 FLEXPEN) from 28Apr2017 at 100 U/ml (8+8) subcutaneously for diabetes, acetylsalicylic acid (TROMBYL) tablet from 14Mar2014 at 75 mg once daily via oral route for diabetes, ezetimibe (EZETIMIBE SANDOZ) tablet from 24Apr2015 at 10 mg once daily via oral route for hyperlipidemia, paracetamol (ALVEDON) film-coated tablet 1000 mg four times daily for pain due to spinal stenosis, alfacalcidol (ETALPHA) capsule from 09Nov2018 at 0.25 microgram via oral route for vitamin D supplementation; calcium chloride dihydrate, icodextrin, magnesium chloride hexahydrate, sodium chloride, sodium lactate (EXTRANEAL) intraperitoneal from 13Oct2016 for peritoneal dialysis and treatment of renal failure; calcium chloride dihydrate, glucose, magnesium chloride, sodium bicarbonate, sodium chloride, sodium lactate (PHYSIONEAL) intraperitoneal from 13Oct2016 for peritoneal dialysis, treatment for renal failure; macrogol 3350, potassium chloride, sodium bicarbonate, sodium chloride (MOVICOL) powder for oral solution from 28Nov2016 orally at 1 dose form as needed for constipation, propylene glycol (PROPYLESS) cutaneous emulsion from 04Dec2017 cutaneously as needed to soften skin, hydroxyzine hydrochloride (ATARAX) film-coated tablet from 24Mar2017 via oral route at 25 mg 0.5-1 tablet daily as needed for itching due to renal failure, hypromellose (ARTELAC) eyedrops from 20Sep2017 at 1-2 dose forms as needed, furosemide (FURIX) tablet from 28Oct2018 via oral route at 500 mg twice daily for fluid retention due to renal failure and zopclone (IMOVANE) tablet from 07Feb2019 via oral route at 7.5 mg at 0.5-1 tablet daily as needed for sleeping, sevelamer (SEVELAMER SANDOZ) initiated on 09May2017 at 2.4 g 3 times daily for hyperphosphatemia. No changes were made to the concomitant drugs prior to the admission.

On 04May2019, the subject experienced NSTEMI which required hospitalization. On 06May2019, the subject experienced cardiac failure which was considered as non-serious by the investigator. The clinical course was as follows: the subject came to the hospital on 04May2019 because of chest pain, troponin increased and the diagnosis of non-ST-elevation myocardial infarction (NSTEMI) was made. An echocardiogram on 06May2019 demonstrated mild cardiac failure. Later echocardiograms also had showed relatively similar results. He underwent coronary angiography and PCI on 06May2019, proximal LAD stenosis a DES was implanted with good result. Subject was admitted to hospital from 04May2019 to 07May2019, the event was not threatening.

The subject also received clopidogrel (PLAVIX) at admission on 04May2019, via oral route of administration at 75 mg 4 times daily for NSTEMI; glyceryltrinitrate (GLYTRIN) as needed from 05May2019 and bisoprolol (BISOPROLOL) at 2.5 mg once daily from 07May2019, both drugs were started after admission for NSTEMI; glyceryltrinitrate (GLYTRIN) at 0.4 mg/dos vial oral route for ischemic heart failure from 06May2019; heparin sodium (HEPARIN LEO) was taken at 5000 ie/ml via intravenous (IV) due to renal failure and anticoagulant, NSTEMI coronary from 06May2019; glucose (GLUCOS BAXTER VIAFLO) was taken at 50 mg/ml as infusion fluid via IV from 06May2019; adenosine (ADENOSIN LIFE) medical was taken at 5mg/ml for coronary angiography via IV from 06May2019; lidocaine hydrochloride (XYLOCAIN) was taken at 10mg/ml for coronary angiography via IV from 06May2019; iodixanol (VISIPAQUE) was taken at 320mg i/ml for contrast for coronary angiogram via IV from 06May2019; sodium chloride (NATRIUMKLORID BAXTER) at 9 mg/ml as infusion fluid via IV from 06May2019.

On 06May2019, the subject underwent coronary angiography and percutaneous coronary intervention (PCI) with left anterior descending artery (LAD) on a drug-eluting stent (DES) was performed with good result. No chest pain was reported after the procedure. Laboratory or diagnostic results included the following: B-Haemoglobin: 118 g/l on 05Feb2019; 110 g/l on 18Mar2019; 117 g/l on 23Apr2019; 116 g/l on 04May2019 (morning) and 117 g/l on 04May2019 (evening). Haematocrit (B-EVF): 0.36 on 05Feb2019; 0.34 on 18Mar2019; 0.37 on 23Apr2019; 0.36 on 04May2019 (morning) and 0.36 on 04May2019 (evening). No units provided. Red blood cells: 3.7 on 05Feb2019; 3.6 on 18Mar2019; 3.9 on 23Apr2019; 3.9 on 04May2019 (morning) and 4.0 on 04May2019 (evening). P-CRP: 2 on 05Feb2019; 4 on 18Mar2019; 5 on 23Apr2019; 4 on 04May2019 (morning) and 4 on 04May2019 (evening). No units provided. B-Leukocytes: 8.5 on 05Feb2019; 8.4 on 18Mar2019; 8.0 on 23Apr2019; 7.7 on 04May2019 (morning) and 8.9 on 04May2019 (evening). No units provided. Results for reticulocytes, differential blood count and BSR (blood sedimentation rate) were not available. Diagnostic test results performed to establish the diagnosis/adverse reaction included ECG readings: ECG 04May2019: Pathological ECG, atrium-sensed ventricular-paced rhythm. Ventricular frequency: 60 S/M PQ time: 170ms; QRS duration 184 ms, QT/QTc 524/524ms; PRT axis 68 -66 112. Echocardiography: 06May2019: EF 40-49%. Transthoracic Echocardiography: Sinus rhythm 61/min. Acceptable transmission conditions. Dimension and Function: Left ventricle: VKd 44 mm. Septum 18mm. Posterial wall 13mm. Systolic function: EF 40% visually, EF biplan Simpson 39% (more than 55%). Global Longitudinal Strain -10.6%. SV index 56mL/m2. Regional function: General hypokinesia, mostly pronounced apically, inferoseptally and inferior. Right ventricle: Visually of normal size. Normal systolic function, TAPSE 21 mm (more than 17 mm). Atrium: left 50 mgl/m2 (less than 34), right 21 cm2 (less than 18) / 33 ml/m2 (less than 32). Valves: Aorta ascendens was slightly dilated (sinus 43mm), ascendens 40mm). Aortic valve was tricuspid had increased echogenicity. Aortasclerosis without stenosis. Moderate insufficiency. Mitralis valve was morphologically and functionally normal. Moderate calcification in the posterior segment of anulus. Moderate insufficiency. Tricuspidalis valve was morphologically intact with sligth insufficiency. Hemodynamics: Disturbance in relaxation with normal left-sided filling pressures in the atrium (E/E 11, E/A less than 1, S more than D) Systolic right ventricle pressure can not be calculated. CVP 5 mmHg. No pericardial

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

fluid. Assessment: At least moderate escentric hypertrophic left ventricle with moderately impaired EF 40%. Normal sized right ventricle with normal function. Aortasclerosis without stenosis. Mild aortic insufficiency. Diagnosis according to ICD-10; 1442 Atrioventricular block, total. R074 Chest pain, unspecifed. Troponin T was 417 on 04May2019 at 07:43 am; 727 on 04May2019 at 10:14 am; 1570 on 04May2019 at 18:13 pm and 1580 on 04May2019 at 19:01 pm; 1420 on 05May2019 and 1360 on 07May2019. Creatinine kinase was not available. Coronary angiography: 06May2019: slight atheromatosis, dominating Cx system. LAD had a moderate excentric plaque ostially and a moderate stenosis proximally. Pressure measurement in LAD with ic adenosine/nitro shows FFR 0.75 ie singificant stenosis. The action taken in response to the event for epoetin zeta was dose not changed. Outcome of the event NSTEMI was recovered on 07May2019 with no chest pain. Outcome of the event cardiac failure was not recovered.

The investigator considered there was not a reasonable possibility that the events NSTEMI and cardiac failure were related to the study medication and concomitant medications.

Follow-up (15Nov2019): New information reported includes: suspect drug details, relevant medical history, concomitant medications, lab data, treatment received, hospitalization date and subject clinical courses.

Follow-up (13Dec2019): New information reported includes: reaction data (additional non serious adverse event 'cardiac failure' added; clinical course); additional relevant tests and medications.

Amendment: This follow-up report is being submitted to amend previously reported information: updated the start date for study drug; clinical course updated.

Case Comment: In agreement with the investigator, the Company considered there was not a reasonable possibility that the reported events, non-ST-elevation myocardial infarction (NSTEMI) and cardiac failure, were related to the study drug epoetin zeta (RETACRIT). The events were most likely due to the subject's underlying cardiovascular conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	06-MAY-2019	Angiogram	slight atheromatosis, dominating Cx system...	
2	05-FEB-2019	C-reactive protein	2	
3	18-MAR-2019	C-reactive protein	4	
4	23-APR-2019	C-reactive protein	5	
5	04-MAY-2019	C-reactive protein	4	
6	04-MAY-2019	C-reactive protein	4	
7	04-MAY-2019	Echocardiogram	Pathological ECG, atrium-sensed ventricular-paced	
8	06-MAY-2019	Echocardiogram	EF 40-49%	
9		Electrocardiogram	relatively similar results	
10	04-MAY-2019	Electrocardiogram	Pathological ECG, atrium sensed chamber packaged..	
11	06-MAY-2019	Electrocardiogram	mild cardiac failure	
12	05-FEB-2019	Haematocrit	0.36	
13	18-MAR-2019	Haematocrit	0.34	
14	23-APR-2019	Haematocrit	0.37	
15	04-MAY-2019	Haematocrit	0.36	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
16	04-MAY-2019	Haematocrit	0.36	
17	05-FEB-2019	Haemoglobin	118 g/l	
18	18-MAR-2019	Haemoglobin	110 g/l	
19	23-APR-2019	Haemoglobin	117 g/l	
20	04-MAY-2019	Haemoglobin	116 g/l	
21	04-MAY-2019	Haemoglobin	117 g/l	
22	05-FEB-2019	Red blood cell count	3.7	
23	18-MAR-2019	Red blood cell count	3.6	
24	23-APR-2019	Red blood cell count	3.9	
25	04-MAY-2019	Red blood cell count	4.0	
26	04-MAY-2019	Red blood cell count	3.9	
27		Troponin T	increased	
28	04-MAY-2019	Troponin T	1580	
29	04-MAY-2019	Troponin T	1570	
30	04-MAY-2019	Troponin T	417	
31	04-MAY-2019	Troponin T	727	
32	05-MAY-2019	Troponin T	1420	
33	07-MAY-2019	Troponin T	1360	
34	05-FEB-2019	White blood cell count	8.5	
35	18-MAR-2019	White blood cell count	8.4	
36	23-APR-2019	White blood cell count	8.0	
37	04-MAY-2019	White blood cell count	8.9	
38	04-MAY-2019	White blood cell count	7.7	

13. Relevant Tests

Troponin 04May2019: 07:43 417; 10:14: 727; 18:13: 1570; 19:01: 1580
Coronary angiography(06May2019): slight atheromatosis, dominating Cx system. Left anterior descending artery (LAD) has a moderate excentric plaque ostially and a moderate stenosis proximally. Pressure measurement in LAD with ic adenosine/nitro shows FFR 0.75 ie singificant stenosis.

ADDITIONAL INFORMATION

13. Relevant Tests

Echocardioagraphy (06May2019): Ejection fraction (EF) 40-49%. Transthoracic Echocardiography: Sinus rhythm 61/min. Acceptable transmission conditions. Dimension and Function: Left ventricle: VKd 44 mm. Septum 18mm. Posterial wall 13mm. --Systolic function: EF 40% visually, EF biplan Simpson 39% (more than 55%). Global Longitudinal Strain -10.6%. SV index 56mL/m2. -- Regional function: General hypokinesia, mostly pronounced apically, inferoseptally and inferior. Right ventricle: Visually of normal size. Normal systolic function, TAPSE 21 mm (more than 17 mm). Atrium: left 50 mgl/m2 (less than 34), right 21 cm2 (less than 18) / 33 ml/m2 (less than 32). Valves: Aorta ascendens was slightly dilated (sinus 43mm, ascendens 40mm). Aortic valve is tricuspid has increased echogenicity. Aortasclerosis without stenosis. Moderate insufficiency. Mitralis valve was morphologically and functionally normal. Moderate calcification in the posterior segment of anulus. Moderate insufficiency. Tricuspidalis valve is morphologically intact with sligth insufficiency. Hemodynamics: Disturbance in relaxation with normal left-sided filling pressures in the atrium (E/E 11, E/A less than 1, S more than D). Systolic right ventricle pressure can not be calculated. CVP 5 mmHg. No pericardial fluid. Assessment: At least moderate escentric hypertrophic left ventricle with moderately impaired EF 40%. Normal sized right ventricle with normal function. Aortasclerosis without stenosis. Mild aortic insufficiency. Diagnosis according to ICD-10; 1442 Atrioventricular block, total. R074 Chest pain, unspecifed.
ECG (04May2019): Pathological ECG, atrium-sensed ventricular-paced rhythm. Ventricular frequency: 60 S/M PQ time: 170millisecond; QRS duration 184 ms, QT/QTc 524/524millisecond; PRT axis 68 -66 112.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) NOVOMIX 30 Flexpen (INSULIN ASPART, INSULIN ASPART PROTAMINE (CRYSTALLINE)) Solution for injection ; 28-APR-2017 / Ongoing

#6) EXTRANEAL (CALCIUM CHLORIDE DIHYDRATE, ICODEXTRIN, MAGNESIUM CHLORIDE HEXAHYDRATE, SODIUM CHLORIDE, SODIUM LACTATE) ; 13-OCT-2016 / Ongoing

#7) PHYSIONEAL (CALCIUM CHLORIDE DIHYDRATE, GLUCOSE, MAGNESIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE, SODIUM LACTATE) ; 13-OCT-2016 / Ongoing

#8) MOVICOL [MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CH (MACROGOL 3350, POTASSIUM CHLORIDE, SODIUM BICARBONATE, SODIUM CHLORIDE) Powder for oral solution ; 28-NOV-2016 / Unknown

#9) PROPYLESS (PROPYLENE GLYCOL) Cutaneous emulsion ; 04-DEC-2017 / Unknown

#10) ATARAX [HYDROXYZINE HYDROCHLORIDE] (HYDROXYZINE HYDROCHLORIDE) Film-coated tablet ; 24-MAR-2017 / Ongoing

#11) ARTELAC [HYPROMELLOSE] (HYPROMELLOSE) Eye drops ; 20-SEP-2017 / Unknown

#12) FURIX [FUROSEMIDE] (FUROSEMIDE) Tablet ; 28-OCT-2018 / Ongoing

#13) IMOVANE (ZOPICLONE) Tablet ; 07-FEB-2019 / Ongoing

#14) SEVELAMER SANDOZ (SEVELAMER CARBONATE) ; 09-MAY-2017 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
OCT-2016 to Ongoing	Relevant Med History	Peritoneal dialysis (Peritoneal dialysis);
19-JAN-2019 to Ongoing	Relevant Med History treated with pacemaker	Atrioventricular block (Atrioventricular block);
Unknown to Ongoing	Relevant Med History	Pacemaker insertion (cardiac) (Cardiac pacemaker insertion);
1990 to Ongoing	Relevant Med History	Hypertension (Hypertension);
23-MAR-2018 to Ongoing	Relevant Med History	Spinal stenosis (Spinal stenosis);
27-APR-2010 to Ongoing	Relevant Med History	Hyperlipidemia (Hyperlipidaemia);

Mfr. Control Number: 2019431417

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
04-MAY-2019 to Ongoing	Relevant Med History diagnosed at hospitalization	Ischaemic heart disease (Myocardial ischaemia);

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15.3.12.2.2 Treatment-Related Serious Adverse Event (Adverse Drug Reaction) Narratives

Narratives are provided for treatment-related serious adverse event (adverse drug reaction):

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
It-093-0008	2150382	Dermatitis atopic

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SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	22	MAY	1943	70 Years	Male	64.00 kg	22	AUG	2013	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Atopic dermatitis [Dermatitis atopic]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from Non-Interventional Study source for protocol EPOE-09-11.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000/15 days	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 10-JUN-2013 / 16-AUG-2013	#1) 68 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
20-JUN-2013 to Unknown	Relevant Med History	Renal failure (Renal failure)
	30Oct2013: onset of dialysis	
20-JUN-2013 to Unknown	Relevant Med History	Hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2150382

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-MAR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Italy, administered subcutaneously for the treatment of renal anaemia. This report describes a case of dermatitis. This non-serious case from an investigator (reference: IT-093-0008) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; frequency and batch number not reported) for renal anaemia on an unknown date. Medical history included renal failure since 20Jun2013 with 30Oct2013: onset of dialysis and hypertension since 20Jun2013 and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced dermatitis. Action taken with the suspect drug, treatment and outcome of the adverse event were not reported. The reporter's causality assessment between the event of dermatitis and epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number, date of expiry, and previous exposure of patient to other biosimilars. 14-Feb-2014: Additional information was received from the investigator. Follow-up report created to reflect additional information regarding suspect drug, patient details, adverse event, medical history, reporter's causality assessment and seriousness criteria. The case was upgraded to serious and was considered medically significant. The adverse event was changed to atopic dermatitis. Batch number was unknown. The patient was a 70-year-old male patient (weight: 64 kg; height: 168 cm). The patient had no known drug hypersensitivities and no history of drug dependencies. The patient did not receive the suspect drug before. On 10-Jun-2013, the patient received Retacrit (4000/15 days). The suspect drug was discontinued on 16-Aug-2013. On 22-Aug-2013, the patient experienced atopic dermatitis described as vesicles which spread all over the body, followed by abundant desquamation of the skin. Medical intervention included administration of cortisones and antihistamines (doses and routes of administration not reported). Outcome of the adverse event was fully recovered on an unknown date. It was reported that the event had a duration of 2 months. It was also reported that the reaction reappeared upon rechallenge. The reporter's causality assessment between the event of atopic dermatitis and epoetin zeta was probable. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. The subject was withdrawn from the study and no information was available as the subject did not return to the site after withdrawal. The subject died after completing the study. The subject died on 09May2017 from IMA, reported to be an acute myocardial infarction, and no autopsy was done.

This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

Follow-up (26Mar2019): Updates subject data, medical history, subject status, and death data.

Case Comment: Based on the compatible temporal association and given the fact that the reaction reappeared upon rechallenge, the Company considers the reported event atopic dermatitis is possibly related to suspect drug epoetin zeta. The impact of this report on the benefit/risk profile of the Pfizer product is evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators, as appropriate.

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15.3.12.2.3 Serious Adverse Event Resulting in Permanent Discontinuation Narratives

Narratives are provided for serious adverse event resulting in permanent discontinuation, includes serious adverse events of special interest or treatment-related serious adverse event (adverse drug reaction) only:

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
Fin-001-0005**	2016557897	Drug ineffective
Ge-048-0037**	2963426	Basal ganglia haemorrhage
Ge-093-0185**	2017269786	Coronary artery thrombosis
Ge-094-0019**	2017064895	Cerebral haemorrhage
Ge-115-0015*	998219	Arterial thrombosis
Ge-152-0025*	2651469	Cerebral infarction; Myocardial infarction
Ge-463-0008*	2021971	Basal ganglia haemorrhage; Subdural haematoma
Gr-002-0019*	2693195	Acute myocardial infarction
Gr-002-0025*	2797025	Myocardial infarction
Gr-045-0051*	2018212348	Myocardial infarction
Gr-051-0090*	2017244407	Myocardial infarction
It-087-0004**	1617854	Drug ineffective
It-116-0032**	2876300	Aplasia pure red cell; Drug ineffective
Sw-011-0023*	2016443936	Myocardial infarction
Sw-011-0028*	2018182041	Cerebral haemorrhage

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*Narrative for these patients appear in Section 15.3.12.1 – Death Narratives.

**Narrative for these patients appear in Section 15.3.12.2 – Serious Adverse Event of Special Interest Narratives.

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15.3.12.3.1 Non-Serious Adverse Event of Special Interest Narratives

Below is the list of non-serious adverse events of special interest cases:

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
Ge-048-0016	2104804	Embolism
Ge-083-0006*	1793228	Cerebral infarction
Ge-097-0007	2119625	Drug ineffective
Ge-097-0016	2119610	Drug ineffective
Ge-463-0008*	2021971	Drug ineffective
Gr-017-0020	2362260	Drug ineffective
It-116-0042	2017455775	Transient ischaemic attack
Sw-005-0004	1426858	Drug ineffective
Sw-005-0010	1426871	Drug ineffective
Sw-005-0016	1426845	Drug ineffective
Sw-005-0019	1430483	Drug ineffective

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*Narrative for this patient appears in Section 15.3.12.1– Death Narratives.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SWEDEN	05	JUN	1961	51 Years	Male	102.00 kg	24	MAY	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). This report describes a case of lack of efficacy. This non-serious report from a
physician (SWE-005-0016) describes a 51-year-old male patient who started treatment with Retacrit (epoetin zeta; 10000 IU, twice a week, subcutaneous, formulation and batch number not reported) for low hemoglobin on 03-Mar-2011.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 10000 IU, UNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low hemoglobin (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 03-MAR-2011 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL NYCO (ALLOPURINOL) Tablet ; 03-NOV-2010 / Unknown
#2) ARANESP (DARBEPOETIN ALFA) Solution for injection in pre-fille
#3) ATACAND (CANDESARTAN CILEXETIL) Tablet ; 09-JUL-2009 / Unknown
#4) BETOLVEX /00056201/ (CYANOCOBALAMIN) Tablet ; 11-NOV-2011 / Unknown
#5) COSMOFER (IRON DEXTRAN) ; 03-MAR-2011 / Unknown
#6) DEXOFEN /00018803/ (DEXTROPROPOXYPHENE NAPSILATE) Tablet

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History 26-Apr-2012	Hemodialysis (Haemodialysis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1426845

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-SEP-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included hemodialysis and thyroid surgery. The patient was not exposed to any other erythropoietin-stimulating-agent (ESA) at any time. Concomitant medications were not reported. On 03-Mar-2011, the patient started treatment with epoetin zeta. On 14-May-2012, the patient received epoetin zeta and haemoglobin was at 106 g/L on 15-May-2012. On 18-May-2012, the patient also received epoetin zeta. The last dose of epoetin zeta prior to the event was given on 21-May-2012. There has been no change in dose within 3 months prior to the event. On 24-May-2012, the patient experienced lack of efficacy with epoetin zeta. Haemoglobin on 28-May-2012 was at 106 g/L. It was reported that hemoglobin was judged to be too low prior to the thyroid surgery. Treatment of the adverse event and action taken with epoetin zeta was not reported. The outcome of the event of lack of effect was not recovered. The reporter's causality assessment of the event of lack of efficacy in relation to epoetin zeta was unlikely. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number and date of expiry. English translation of foreign source document was received on 09-Oct-2012. Follow-up report created to reflect new information patient's medical history and concomitant medications. The patient initiated dialysis on 26-Apr-2012. Concomitant medications included Novorapid Flexpen Injection liquid, solution in pre-filled syringe 100 U/ML (insulin aspart; 15 units in the morning, at lunch-time, and in the evening; subcutaneous); Insulatard Flexpen Injection liquid, suspension in pre-filled injection pens 100 IU/ml (isophane human; 20 units at night; subcutaneous); Innohep Injection liquid, solution 10,000 anti-Xa IU/ml (tinzaparin; 0.8 ml, 0 units in conjunction with start of dialysis in 3 hours dialysis; intravenous); Cosmofer Injection/Infusion liquid, solution 50 mg/ml (0 ml every week; oral); Aranesp Injection liquid, solution, pre-filled syringes 100 mcg (1 syringe every week; intravenous); Atacand tablet 16 mg (candesartan; 0.5 tablet in the evening, oral); Fenuril cream (1 application twice daily; also reported as oral); Mimpara coated tablet 30 mg and 60 mg (1 tablet once daily; oral); Zemplar injection liquid, solution 5 microg/ml (1 ml, 5 mcg, every week, intravenous); Siduro gel 2.5% (1 application twice daily, also reported as oral); Pulmicort Turbuhaler Inhalation powder 200 mcg/dose (1 inhalation twice daily; inhalation); Resonium powder for oral/rectal suspension (polystyrene sulfonate; 15 ml on non-dialysis days; oral); Renvela coated tablet 800 mg (sevelamer carbonate; 2-3 tablets thrice daily; oral); Renvela Powder for oral suspension 2.4 g (sevelamer carbonate; 1 pouch thrice daily as needed, max of 3 pouches in 24 hours, oral); Osvarem Coated tablet 435 mg/235 mg (calcium acetate; 1 tablet thrice daily, oral, to be swallowed with whole meals); omeprazole Sandoz enteric capsule hard 20 mg (1 capsule as needed, oral); Laktulos Alternova Syrup 667 mg/ml (lactulose; 15 ml as needed, oral); NovoRapid Injection liquid, solution 100 U/ml (4-6 U as needed; subcutaneous); Ketogan Novum Tablet (ketobemidone hydrochloride; 0.5 tablet as needed, oral), Ketogan Novum Injection liquid, solution 5 mg/ml (ketobemidone hydrochloride; 0.5 ml as needed, subcutaneous); Panodil coated tablet 500 mg (paracetamol; 2 tablets four times daily as needed, oral); Ventoline Evohaler inhalation spray, suspension 0.1 mg/dose (salbutamol sulphate; 1 inhalation as needed, inhalation); Loratadine Ratiopharm tablet 10 mg (1 tablet as needed, oral) (all for unknown indications); Trombyl tablet 75 mg (acetylsalicylic acid; 1 tablet once daily, oral) as blood thinner; Betolvex coated tablet 1 mg (cyanocobalamine; 1 tablet once daily, oral) as vitamin B supplement; Folacin tablet 5 mg (folic acid; 2 tablets once daily, oral) as vitamin supplement; Emconcor CHF Coated tablet 10 mg (bisoprolol; 0.5 tablet twice daily, oral) for blood pressure; simvastatin Ranbaxy coated tablet 10 mg (1 tablet in evening, oral) for blood lipids; allopurinol Nycomed tablet 100 mg (1 tablet daily, oral) for gout; OxyNorm capsule, hard 5 mg (oxycodone; 1 capsule as needed, max of 3 capsules per 24 hours, oral, to take with paracetamol) and Dexofen tablet 50 mg (dexketoprofen; 1 -2 tablets as needed, max of 3 tablets per 24 hours, oral) for pain. The patient was discharged on 20-Sep-2012. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product: batch number and date of expiry. Follow up information received on 14-Mar-2013 from the physician. Follow up report was created to reflect new information regarding patient's medical history. The patient was exposed to other erythropoetin-stimulating agent Eprex from 08-Dec-2008 until 03-Mar-2011 at a dose of 10000 E. Proprietary Medicinal Product names of Novorapid, Insulatard, Innohep, Trombyl, Cosmofer, Betolvex, Folacin, Aranesp, Emconcor, Atacand, Simvastatine Ranbaxy, Fenuril, Mimpara, Zemplar, Siduro, Allopurinol Nyco, Pulmicort Turbuhaler, Resonium, Renvela, Omeprazol Sandoz, Laktulos, Oxynorm, Ketogan Novum, Panodil, Dexofen, Ventoline, and Loratadin Ratiopharm were selected. In the narrative, the active ingredients of Novorapid, Insulatard, Innohep, Trombyl, Cosmofer, Betolvex, Folacin, Aranesp, Emconcor, Atacand, Simvastatine Ranbaxy, Fenuril, Mimpara, Zemplar, Siduro, Allopurinol Nyco, Pulmicort Turbuhaler, Resonium, Renvela, Omeprazol Sandoz, Laktulos, Oxynorm, Ketogan Novum, Panodil, Dexofen, Ventoline, and Loratadin Ratiopharm should not be included as the information had not been provided by the reporter Time from first and last dose to onset were populated for epoetin zeta. Action taken with suspect drug was populated in the structured field. Dosage forms for epoetin zeta, Novorapid, Innohep, Trombyl, Betolvex, Folacin, Aranesp, Emconcor, Atacand, Simvastatine Ranbaxy, Fenuril, Mimpara, Zemplar, Siduro, Allopurinol Nyco, Pulmicort Turbuhaler, Renvela, Omeprazol Sandoz, Laktulos, Oxynorm, Ketogan Novum, Panodil, Dexofen, and Loratadin Ratiopharm were populated. Frequency of Pulmicort Turbuhaler was structured as twice daily (previously structured as once every two days). Frequency of Panodil was structured as four times daily (previously structured as once every four days). 18-Sep-2013: Follow up report was received from the same reporter. Follow up report was created to reflect additional information regarding the patient's medical history and to correct the patient identification number. Patient identification number for this report is Sw-005-0016. The patient did not complete the study and was withdrawn from the study on 24-May-2012 due to lack of efficacy. There was no blood sample retained at the end of the study.

Case Comment: Overall case causality: Probably Not Noting the history of hemodialysis, consider extent of underlying anemia as causative factor, rather than lack of efficacy of suspect drug. Overall case causality (Follow-up 22 Oct 2012): Probably Not No change in assessment Follow-up (23 March 2013): New information noted, but does not warrant change in previous assessment. - N. Gonzales (23 March 2013) Follow-up: No change in previous assessment. - N. Gonzales

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(23 Sep 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	15-MAY-2012	Haemoglobin	106 g/l	
2	28-MAY-2012	Haemoglobin	106 g/l	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) ARANESP (DARBEPOETIN ALFA) Solution for injection in pre-filled syringe ; 24-MAY-2012 / Unknown

#6) DEXOFEN /00018803/ (DEXTROPROPOXYPHENE NAPSILATE) Tablet ; 03-DEC-2010 / Unknown

#7) EMCONCOR (BISOPROLOL FUMARATE) Tablet ; 11-SEP-2007 / Unknown

#8) FENURIL (SODIUM CHLORIDE, UREA) Cream ; 21-OCT-2008 / Unknown

#9) FOLACIN /00024201/ (FOLIC ACID) Tablet ; 11-SEP-2007 / Unknown

#10) INNOHEP (TINZAPARIN SODIUM) Solution for injection ; 01-DEC-2011 / Unknown

#11) INSULATARD /00646002/ (INSULIN HUMAN INJECTION, ISOPHANE) ; 15-FEB-2012 / Unknown

#12) KETOGAN NOVUM (KETOBEMIDONE HYDROCHLORIDE) Tablet ; 13-NOV-2010 / Unknown

#13) KETOGAN NOVUM (KETOBEMIDONE HYDROCHLORIDE) Solution for injection ; 13-NOV-2010 / Unknown

#14) LAKTULOS (LACTULOSE) Syrup ; 07-OCT-2009 / Unknown

#15) LORATADIN RATIOPHARM (LORATADINE) Tablet ; 03-MAY-2012 / Unknown

#16) MIMPARA (CINACALCET HYDROCHLORIDE) Tablet ; 10-MAR-2010 / Unknown

#17) NOVORAPID (INSULIN ASPART) Solution for injection in pre-filled syringe ; 02-SEP-2009 / Unknown

#18) NOVORAPID (INSULIN ASPART) Solution for injection ; 11-NOV-2010 / Unknown

#19) OMEPRAZOL SANDOZ /00661201/ (OMEPRAZOLE) Capsule ; 07-OCT-2009 / Unknown

#20) OXYNORM (OXYCODONE HYDROCHLORIDE) Capsule ; 28-JAN-2011 / Unknown

#21) PANODIL (PARACETAMOL) Tablet ; 01-DEC-2011 / Unknown

#22) PULMICORT TURBUHALER (BUDESONIDE) Inhalation powder ; 03-MAY-2012 / Unknown

#23) RENVELA (SEVELAMER CARBONATE) Tablet ; 03-JUN-2010 / Unknown

#24) RENVELA (SEVELAMER CARBONATE) ; 14-APR-2011 / Unknown

#25) RESONIUM (SODIUM POLYSTYRENE SULFONATE) ; 17-OCT-2008 / Unknown

#26) SIDURO (KETOPROFEN) Gel ; 03-MAY-2012 / Unknown

#27) SIMVASTATINE RANBAXY (SIMVASTATIN) Tablet ; 27-MAY-2009 / Unknown

#28) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; 11-SEP-2007 / Unknown

#29) VENTOLINE /00139501/ (SALBUTAMOL) ; 03-MAY-2012 / Unknown

Mfr. Control Number: 1426845

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#30) ZEMPLAR (PARICALCITOL) Solution for injection ; 25-AUG-2010 / Unknown

#31) CALCIUM ACETATE (CALCIUM ACETATE) Tablet ; 01-DEC-2011 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. Medical history included hemodialysis and thyroid surgery. The patient was not exposed to any other erythropoietin-stimulating-agent (ESA) at any time. English translation was received on 09-Oct-2012: The patient initiated dialysis on 26-Apr-2012. Follow up report was received on 14-Mar-2013 regarding patient's medical history: The patient was exposed to other erythropoetin-stimulating agent Eprex from 08-Dec-2008 until 03-Mar-2011 at a dose of 10000 E. 18-Sep-2013: Follow up information was received regarding the patient's medical history. The patient did not complete the study and was withdrawn from the study on 24-May-2012 due to lack of efficacy. There was no blood sample retained at the end of the study
Unknown	Relevant Med History	Thyroid operation (Thyroid operation);
08-DEC-2008 to 03-MAR-2011	Past Drug Event	EPREX (EPREX); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	21	AUG	1953	58 Years	Male	104.00 kg	04	MAR	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This is a Post-Authorisation Safety Cohort Observation of Retacrit (epoetin zeta) administered subcutaneously for the treatment of renal anaemia (PASCO II). This report from Sweden describes a case of lack of efficacy. This non-serious
case from a physician (ref: SWE-005-0004) describes a 59-year-old male patient (weight: 104 Kg; height: 175 cm) who received Retacrit pre-filled syringe (epoetin zeta; 10,000 IU, once per week from 03-Oct-2011 to 04-Mar-2012 then 14,000

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low Hb (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 03-OCT-2011 / 04-MAR-2012

19. THERAPY DURATION
#1) 154 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) BEHEPAN /00056201/ (CYANOCOBALAMIN) Tablet ; 12-APR-2007 / Unknown
#2) CIPRALEX /01588502/ (ESCITALOPRAM OXALATE) Tablet ; 16-APR-2008 / Unknown
#3) COZAAR (LOSARTAN POTASSIUM) Tablet ; 12-APR-2007 / Unknown
#4) INSUMAN COMB (INSULIN HUMAN, INSULIN HUMAN INJECTION
#5) METOPROLOL SANDOZ /00376902/ (METOPROLOL TARTRATE) ; 12-MAR-2009 / Unknown
#6) NOVORAPID (INSULIN ASPART) Solution for injection ; 27-AUG-2009 / Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History	Hemodialysis (Haemodialysis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1426858

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-MAR-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

IU per week from 29-Feb-2012 to 04-Mar-2012, subcutaneous; batch number not reported) for low Hb. Medical history included hemodialysis. The patient was not exposed at any time to any other erythropoeitin stimulating agent (ESA).
However, it was also reported that the patient received Eprex (epoetin alfa; 10,000 IU, subcutaneous) from 27-Mar-2008 to 16-May-2008 and 07-Oct-2008 to 16-Jan-2010. The patient did not experience any episode of lack of effect and did not develop anti-erythropoeitin anti-bodies during treatment with any other ESA. Concomitant medications included prednisolon Pfizer 5 mg (3 tablets, once daily, oral) and prednisolon Pfizer 2.5 mg tablet (1 tablet, once daily, oral), Cipralex 15 mg coated tablet (escitalopram; 1 tablet, once daily, oral), Novorapid 100 IU/ml (insulin aspart; 4 units subcutaneous, as needed if blood sugar is greater than 20 mmol/L), Panodil coated tablet 500mg (paracetamol; 2 tablets as needed, max of 8 tablets per 24 hours, oral), Thrombyl tablet 160 mg (aspirin; 1 tablet, once daily, oral), omeprazol Pensa enteric capsule 20 mg (1 capsule, once daily, oral), Insuman comb 25 100 IU/ml (insulin injection, biphasic isophane; 80 units in the morning, subcutaneous), metoprolol Sandoz slow release tablet 50 mg (1 tablet, twice a day, oral), Cozaar coated tablet 50 mg (losartan; 1 tablet, once daily, oral), Behepan coated tablet 1 mg (cyanocobalamin; 1 tablet, once daily, oral), and Folacin tablet 5 mg (folic acid; 1 tablet, once daily, oral); all given for unknown indications. On 03-Oct-2011, the patient began treatment with epoetin zeta. On 22-Feb-2012, haemoglobin was at 98 g/L (Normal range: 134-170 g/L). On 23-Feb-2012 at 09:00, haemoglobin (Hb) at 97 g/L On 29-Feb-2012, the dose of epoetin zeta was increased to 14,000 IU per week. On 02-Mar-2012, the patient received the last dose of epoetin zeta (4000 IU) prior to the adverse event.
On 04-Mar-2012, the patient experienced lack of efficacy with epoetin zeta. Monthly testing showed a sinking tendency of hemoglobin. On the same date, epoetin zeta was discontinued and was changed to Aranesp (darbepoetin alfa; 60 mcg, intravenous, prefilled syringe, in conjunction with dialysis). On 27-Mar-2012 at 14:15, blood tests were performed and showed Hb at 102 g/L. Treatment given for the adverse event was not reported. The patient had not yet recovered from the event of lack of efficacy at the time of the report. The reporter's causality assessment between the event of lack of efficacy and epoetin zeta was unlikely. 14-Mar-2013: Additional information was received from the reporter. Follow-up report was created to reflect new information regarding past drug therapy. The patient had previous exposures to erythropoietin-stimulating agents (ESA) which included Aranesp (150 mcg, 1 syringe per week, subcutaneously) from 12-Apr-2007 until 27-Mar-2008 and Eprex (6000 IU, subcutaneous) from 27-Mar-2008 until 17-Jan-2010; both for unknown indications. Additional changes were also made due to recent processing guidelines. Proprietary medicinal product names were selected for Retacrit, Cipralex, Novorapid, Panodil, Thrombyl, Insuman Comb, metoprolol Sandoz, Cozaar, Behepan, Folacin and Eprex. Structured fields for frequency and dosage form were populated for prednisolon Pfizer, Cipralex, Thrombyl, omeprazol Pensa, metoprolol Sandoz, Cozaar, Behepan and Folacin. The structured field for dosage form was populated for Novorapid and Panodil. Time first dose to onset and time last dose to onset for Retacrit were also populated. In the narrative, the product active ingredients for Eprex, Cipralex, Novorapid, Panodil, Thrombyl, Insuman Comb, Cozaar, Behepan and Folacin should not be included as these information were not provided by the reporter.
Data entry corrections were made regarding concomitant medications and reporter contact information. The route of administration of Insuman Comb was subcutaneous (previously entered as oral). The frequency of metoprolol Sandoz was two times daily (previously entered as once every two days). The reporter was unable to provide the following requested information for identification and traceability of the biosimilar product Retacrit (epoetin zeta): batch number. No further information was reported.

Case Comment: Overall case causality: Probably Not Noting reporter's causality of unlikely, consider extent and etiology of patient's anemia as major causative factor, rather than the lack of effect of the suspect dug. Follow-up (25 March 2013): New information noted, but does not warrant change in previous causality assessment. - N. Gonzales

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	22-FEB-2012	Haemoglobin	98 g/l	170 134
2	23-FEB-2012	Haemoglobin	97 g/l	170 134
3	27-MAR-2012	Haemoglobin	102 g/l	170 134

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	10000 IU, Tuesdays in conjuction with dialysis Freq: 1 Week; Interval: 1; Subcutaneous	Low Hb (Haemoglobin decreased)	03-OCT-2011 / 04-MAR-2012; 154 days

Mfr. Control Number: 1426858

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	4000 IU, Fridays in conjunction with dialysis Freq: 1 Week; Interval: 1; Subcutaneous	Low Hb (Haemoglobin decreased)	29-FEB-2012 / 04-MAR-2012; 5 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) INSUMAN COMB (INSULIN HUMAN, INSULIN HUMAN INJECTION, ISOPHANE) ; 05-JUL-2011 / Unknown

#7) PANODIL (PARACETAMOL) ; 12-APR-2007 / Unknown

#8) TROMBYL (ACETYLSALICYLIC ACID) Tablet ; 12-APR-2007 / Unknown

#9) FOLACIN /00024201/ (FOLIC ACID) Tablet ; 12-APR-2007 / Unknown

#10) OMEPRAZOL /00661201/ (OMEPRAZOLE) Capsule ; 15-JUN-2011 / Unknown

#11) PREDNISOLON /00016201/ (PREDNISOLONE) Tablet ; 12-APR-2007 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage were not reported. The patient was not exposed at any time to any other erythropoeitin stimulating agent (ESA). However, it was also reported that the patient received Eprex (epoetin alfa; 10,000 IU, subcutaneous) from 27-Mar-2008 to 16-May-2008 and 07-Oct-2008 to 16-Jan-2010. The patient did not experience any episode of lack of effect and did not develop anti-erythropoeitin anti-bodies during treatment with any other ESA. 14-Mar-2013: Additional information was received from the reporter. Follow-up report was created to reflect new information regarding past drug therapy. The patient had previous exposures to erythropoietin-stimulating agents (ESA) which included Aranesp (150 mcg, 1 syringe per week, subcutaneously) from 12-Apr-2007 until 27-Mar-2008 and Eprex (6000 IU, subcutaneous) from 27-Mar-2008 until 17-Jan-2010; both for unknown indications. Data entry correction was also made regarding patient's race/ethnicity: The patient was Caucasian.
Unknown	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
Unknown	Past Drug Event	EPREX (EPREX); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	SWEDEN	24	SEP	1931	80 Years	Male	70.50 kg	20	APR	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This is a Hospira-Sponsored Post authorisation safety cohort observation (PASCO II) of Retacrit (epoetin zeta), from Sweden, administered subcutaneously, for the treatment of renal anaemia. This report describes a case of lack of efficacy. This case from a physician (reference: SWE-005-0010) describes an 80-year-old male patient (weight 70.5 kg; height 180 cm) who began treatment with Retacrit (epoetin zeta; 10,000 E, once a week, subcutaneous, batch number not known) for low Hb on 19-Sep-2011. The patient did not have any previous exposure to other biosimilars.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 1000 IU, Freq: 1 Week; Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low Hb (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 19-SEP-2011 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) APROVEL (IRBESARTAN) ; 19-AUG-2010 / 19-JUN-2012
#2) ARANESP (DARBEPOETIN ALFA) ; 20-APR-2012 / 21-JUL-2012
#3) EPREX (EPOETIN ALFA) ; 01-OCT-2010 / 19-SEP-2011
#4) ETALPHA (ALFACALCIDOL) ; 07-OCT-2010 / 21-JUL-2012
#5) FINASTERIDE SANDOZ (FINASTERIDE) ; 21-DEC-2010 / 21-JUL-2012
#6) KALCIPOS (CALCIUM CARBONATE) ; 27-OCT-2010 / 21-JUL-2012

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Infection (Infection)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1426871

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-MAR-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Medical history included hemodialysis and an infection (unspecified). Concomitant medications were not reported. On 19-Sep-2011, the patient began treatment with epoetin zeta. On 04-Apr-2012, the patient's haemoglobin was at 94 g/L. Last dose of epoetin prior to the adverse event was given on 13-Apr-2012. On 20-Apr-2012, the patient experienced lack of efficacy. The patient's haemoglobin was low, probably due to iron deficiency. But, no iron treatment was given due to infection. Retacrit was changed to Aranesp (darbepoetin alfa; dose and route of administration not reported) in response to the adverse event. On 14-May -2012, haemoglobin was at 108 g/L. The patient had not yet recovered from the event of lack of efficacy. The reporter's causality assessment between the event of lack of efficacy and epoetin zeta was unlikely. Iron
deficiency was an alternative etiology. English translation of the list of concomitant medications was received on 08-Oct-2012. Follow-up report created to reflect new information regarding the concomitant medications and past drug therapy. Past drug therapy included atropin Mylan 0.5 mg/ml solution in cylinder ampoule (0.5 ml, single dose, subcutaneous) for unknown indication, NovoRapid 100 U/ml injection, liquid solution (insulin aspart; 6 IU, single dose, subcutaneous) for unknown indication, Etalpha 0.25 microg soft capsule (alfacalcidol; 1 capsule on Mondays, Tuesdays, Wednesdays, Thursdays and Fridays/ according to schedule/ once daily, oral) as vitamin D, Kaleorid Depot 750 mg tablet (potassium chloride; 1 tab, twice daily, oral) for unknown indication, Waran 2.5 mg tablet (warfarin; 0 tablet once daily, oral) for prevention of blood clot, Duroferon Depot 100 mg tablet (ferrous sulfate; 0 tablets, once daily, oral) as iron supplement, glucose B. Braun solution for injection (1000 ml, 83.33 ml/h over 12 hours, one infusion for 24 hours, intravenous) for unknown indication, simvastatin Ranbaxy 20 mg coated tablet (0.5 mg, 1 tablet in evening, oral) for blood lipids, Doxyferm 100 mg tablet (doxycycline; two tablets first day then one tablet daily, oral) against airways infections, Kavepenin 1 g coated tablet (phenoxymethylpenicillin potassium; 1 tablet, thrice daily, oral) as anti-infection, Heracillin coated tablet (flucloxacillin, one 750 mg tablet thrice daily, and two 500 mg tablets thirce daily, oral) as anti-infection. Concomitant medications included omeprazol Sandoz 20 mg hard enteric capsule (1 capsule, oral, once daily) for unknown indication, Mycostatin 100,000 IU/ml oral suspension (nystatin; 1 ml, four times daily, oral) as antifungal, Lantus Solostar 100 units/ml solution in pre-filled injection pen (insulin glargine; 5 units, in the morning, subcutaneous) for blood sugar reduction, Lantus Optiset 100 u/ml solution in pre-filled injection pen (insulin glargine; 10 units, daily, subcutaneous) for unknown indication, Etalpha 0.25 microg soft capsule (alfacalcidol; 1 capsule, oral, once daily) for unknown indication, Oralovite tablet (vitamin B and C; 1 tablet, oral, once daily) for vitamin deficiency, Kalcipos 500 mg coated tablet (calcium carbonate; 1 tablet, oral, twice daily) for unknown indication, Waran 2.5 mg tablet (warfarin; dose according to special presription, oral) to prevent blood clot, Venofer 20 mg/ml solution concentrate for injection (iron sucrose injection; 5 ml, every other week, intravenous) for unknown indication, Eprex 10,000 IU/ml solution in pre-filled injection syringe (epoetin alfa; 6000 U, every week, subcutaneous) for unknown indication, Aranesp 60 microg solution in pre-filled injection syringe (darbepoetin alfa; 60 mcg, fridays, in conjunction with dialysis, intravenous) for unknown indication, Aprovel 75 mg coated tablet (irbesartan; 1 tablet, oral, once daily) for kidneys and blood pressure, simvastatin Ranbaxy 10 mg coated tablet (1 tablet, oral, in the evening) for blood lipids, Finasterid Sandoz 5 mg coated tablet and (finasteride; 1 tablet, oral, once daily) for prostate problems. Follow-up information received on 14-Mar-2013 from the investigator. Follow-up report created to reflect new information regarding the patient's medical history. The patient had a previous exposure to other erythropoietin-stimulating agent (ESA) with Eprex (6000 E) from 01-Oct-2010 to 19-Sep-2011. Proprietary Medicinal Product names of epoetin zeta, oralovite, Glucose B. Braun, omeprazol Sandoz, simvastatin Ranbaxy, and
finasteride Sandoz, Kaleorid, Etalpha, Kalcipos, Waran, Mycostatin, Venofer, Eprex, Aranesp, Novorapid, Duroferon depot, Doxyferm, Kavepenin and Heracillin was selected. Frequency of Kaleorid depot was structured as twice daily (previously reported as once every two days). Frequency of Kalcipos was structured as twice daily (previously structured as once every two days). Frequency of Mycostatin was structured as four times daily (previously structured as once every four days). Frequency of Venofer was structured as once every 2 weeks (previously structured as twice in 1 week). Frequency of Heracillin was structured as three times daily (previously structured as once every three days). Time from first and last dose to onset were populated for epoetin zeta, and action taken with epoetin zeta was populated in the structured field. In the narrative, the active ingredients of Kaleorid, Etalpha, Kalcipos, Waran, Mycostatin, Venofer, Eprex, Aranesp, Novorapid, Duroferon depot, Doxyferm, Kavepenin and Heracillin should not be included as the information had not been provided by the reporter. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit (epoetin zeta): Batch number and date of expiry.

Case Comment: Overall case causality: Probably Not Consider patient's underlying iron deficiency as major contributory factor for the anemia. Overall case causality (Follow-up 19 Oct 2012): Probably Not No change in assessment Follow-up (23 March 2013): No change in previous assessment. - N. Gonzales (23 March 2013) Follow-up (27 March 2013): Correction to case does not warrant change in previous assessment. - N. Gonzales (27 March 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	04-APR-2012	Haemoglobin	94 g/l	170 g/L 134 g/L
2	14-MAY-2012	Haemoglobin	108 g/l	170 g/L 134 g/L

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) LANTUS (INSULIN GLARGINE) ; 11-FEB-2009 / 15-MAY-2012

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#8) MYCOSTATIN (NYSTATIN) ; 16-DEC-2011 / 30-DEC-2011

#9) OMEPRAZOL SANDOZ /00661201/ (OMEPRAZOLE) ; 06-APR-2009 / 09-JUL-2012

#10) ORALOVITE (ASCORBIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) ; 16-MAR-2011 / 21-JUL-2011

#11) SIMVASTATIN RANBAXY (SIMVASTATIN) ; 25-MAR-2010 / 21-JUL-2012

#12) VENOFER (SACCHARATED IRON OXIDE) ; 28-OCT-2010 / 19-SEP-2011

#13) WARAN (WARFARIN SODIUM) ; 04-NOV-2010 / 21-JUL-2012

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption and tobacco usage were not reported. Follow-up information received on 14-Mar-2013 from the investigator. Follow-up report created to reflect new information regarding the patient's medical history. The patient had a previous exposure to other erythropoietin-stimulating agent (ESA) with Eprex (6000 E) from 01-Oct-2010 to 19-Sep-2011. Race/Ethnicity: Caucasian
Unknown	Relevant Med History	Hemodialysis (Haemodialysis);
09-APR-2010 to 18-APR-2010	Past Drug Event	DOXYFERM /00055705/ (DOXYFERM /00055705/); Drug Indication: Infection respiratory (Respiratory tract infection)
15-JUN-2010 to 28-OCT-2010	Past Drug Event	DUROFERON (DUROFERON); Drug Indication: Iron supplementation (Mineral supplementation)
09-DEC-2009 to 15-JUN-2010	Past Drug Event	ETALPHA (ETALPHA); Drug Indication: Vitamin D (Vitamin D)
15-JUN-2010 to 07-OCT-2010	Past Drug Event	ETALPHA (ETALPHA); Drug Indication: Vitamin D (Vitamin D)
25-MAR-2009 to 09-DEC-2009	Past Drug Event	ETALPHA (ETALPHA); Drug Indication: Vitamin D (Vitamin D)
31-AUG-2010 to 01-SEP-2010	Past Drug Event	GLUCOSE B. BRAUN (GLUCOSE B. BRAUN); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
01-MAR-2009 to 11-MAR-2009	Past Drug Event	HERACILLIN /00239102/ (HERACILLIN /00239102/); Drug Indication: Infection (Infection)
08-JUL-2011 to 05-AUG-2011	Past Drug Event	HERACILLIN /00239102/ (HERACILLIN /00239102/); Drug Indication: Infection (Infection)
13-MAR-2009 to 27-MAR-2009	Past Drug Event	HERACILLIN /00239102/ (HERACILLIN /00239102/); Drug Indication: Infection (Infection)
30-AUG-2011 to 13-SEP-2011	Past Drug Event	HERACILLIN /00239102/ (HERACILLIN /00239102/); Drug Indication: Infection (Infection)
20-OCT-2010 to 25-OCT-2010	Past Drug Event	KALEORID (KALEORID); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
13-JAN-2011 to 20-JAN-2011	Past Drug Event	KAVEPENIN (KAVEPENIN); Drug Indication: Infection (Infection)

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
04-JUL-2011 to 05-JUL-2011	Past Drug Event	NOVORAPID (NOVORAPID); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
10-DEC-2009 to 25-MAR-2010	Past Drug Event	SIMVASTATIN RANBAXY (SIMVASTATIN RANBAXY); Drug Indication: Lipids (Lipids)
11-FEB-2009 to 10-DEC-2010	Past Drug Event	SIMVASTATIN RANBAXY (SIMVASTATIN RANBAXY); Drug Indication: Lipids (Lipids)
11-FEB-2009 to 08-OCT-2010	Past Drug Event	WARAN (WARAN); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
10-JUN-2011 to 10-JUN-2011	Past Drug Event	ATROPINE (ATROPINE); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN	18	OCT	1966	45 Years	Female	62.50 kg	01	MAR	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a non-serious case of lack
of efficacy. This case from a physician (reference: Sw-005-0019) describes a 45-year-old female patient (weight: 62.5 kg and height: 163 cm) who received Retacrit (epoetin zeta; 10, 000 E from 30-Mar-2011 to 10-Nov-2011 then 4, 000

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 10000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Low Hb (Haemoglobin decreased)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 30-MAR-2011 / 10-NOV-2011

19. THERAPY DURATION
#1) 226 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) COSMOFER (IRON DEXTRAN) Solution for infusion ; 04-JAN-2012 / Unknown
#2) EMLA /00675501/ (LIDOCAINE, PRILOCAINE) Transdermal patch ; 2
#3) GLUCOSE B. BRAUN (GLUCOSE) Solution for infusion ; 10-NOV-2011 / 19-NOV-2011
#4) KALCIDON (CALCIUM CARBONATE) Tablet ; 06-APR-2009 / Unknown
#5) LANZO (LANSOPRAZOLE) Tablet ; 06-APR-2009 / Unknown
#6) LERGIGAN /00033002/ (PROMETHAZINE HYDROCHLORIDE) Tablet
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History	Dialysis (Dialysis)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1430483

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-MAR-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

twice a week from 02-Dec-2011 to 01-Mar-2012, subcutaneous, batch number not reported) for low Hb. The patient was not exposed to any other erythropoietin-stimulating agent (ESA); however it was also reported that the patient received Aranesp 40 mcg (darbepoetin alfa; subcutaneous) from 06-Apr-2009 to 19-Aug-2010. Concomitant medications included Glucos. B. Braun (1000 mL, intravenous), Nutriflex Lipid (1250 mL, intravenous), Rocaltrol capsule (calcitriol, 1 cap in the morning, oral), Oralovite tablet (1 tab in the morning and evening, oral), Kalcidon 250 mg (calcium carbonate, oral), Cosmofer 50 mg/mL (iron dextran, 2 mL each week, intravenous), Tenormin film-coated tablet 25 mg (atenolol, 0.5 tab at bedtime, oral), simvastatin Ranbaxy film coated tablet 20 mg (1 tab in evening, oral), Emla 25mg/25mg (lidocaine and prilocaine; 2 plaster in conjuction with dialysis, dermal), Madopark Quick Mite tablet 50 mg/12.5 mg (benserazide and levodopa; 1 tablet in the morning plus two tablets at bedtime, oral), zopiklon Mylan film-coated tablet 5 mg (1 tablet at bedtime, oral), Lanzo 30 mg (lansoprazole; 1 tab as needed, oral), and Lergigan film-coated tablet 25 mg (promethazine, 1 tab as needed, oral); all for unknown indications. On 30-Mar-2011, the patient started treatment with epoetin zeta. On 01-Mar-2012, the patient experienced lack of efficacy due to lowering of Hb over time. On 01-Mar-2012, laboratory tests at 08:00 showed low hemoglobin of 85 g/L (normal values 117-153), low EVF 0.26 (normal values 0.35-0.46), low erythrocytes 2.9 x10^12/L (normal values 3.9-5.2), MCV 91 fL (normal values 82-98), MCH 29 pg (normal values 27-33), MCHC 323 g/L (normal values 320-360), high thrombocytes 402 x10^9/L (normal values 160-390), and high leukocytes 12.6 x 10^9/L (normal values 3.5-8.8). The last dose of epoetin zeta prior to the event was given on 27-Feb-2012. Retacrit was stopped on 01-Mar-2012 and patient started treatment with Aranesp (darbepoetin alfa injection, 60 mcg each week subcutaneous) on the same day. Outcome of the event was reported as not recovered. The reporter's causality assessment between the event of lack of efficacy and epoetin zeta was possible. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number.
English translation of German text was received on 08-Oct-2012. Follow up report was created to reflect additional information regarding suspect drug and concomitant medications. The patient received epoettin zeta 10, 000 IU every week and 4, 000 IU twice per week Monday plus Friday, in conjuction with dialysis. The concomitant drug Glucose, B.Braun Infusion liquid, solution 50 mg/ml was given at 166ml/h over 6 hours, from 10-Nov-2011 to 11-Nov-2011; at 83.33 ml/h over 12 hours on 17-Nov-2011 to 18-Nov-2011; and then at 125ml/hr over 8 hours, from 18-Nov-2011 until 19-Nov-2011; all at 1 infusion/24 hours. Nutriflex Lipid Peri Infusion liquid, emulsion was given at 104.17 ml/h over 12 hours, 1 infusion/24 hours from 17-Nov-2011 until 20-Nov-2011. The dosage form of Rocaltrol was capsule, soft 0.25 microg and dosage form of Kalcidon was chewable tablet with frequency of 1 chewable tablet thrice daily, to be taken along with meals for elevated phosphate. The dosage form of Cosmofer was injection/infusion liquid, solution 50 mg/ml. Oralovite was given as vitamin supplement. Tenormin was given for heart issues, simvastatin for cholesterol-reducing, Emla medicinal patch as anesthetic patch, zopiklon was given as a sleeping tablet for occasional use, and Lanzo orally-disintegrating tablet for upset stomach. Madoprak Quick Mite mat be swallowed whole or dissolved in liquid, pref. acidic.
Follow up information received on 14-Mar-2013 from the physician. Follow up report was created to reflect new information regarding patient's medical history. The patient was exposed to other erythropoietin-stimulating agents (ESA) Aranesp and Eprex (1000 E; route of administration not reported) from 19-Aug-2010 until 30-Mar-2011. Proprietary Medicinal Product names of Retacrit, Glucose B. Braun, Nutriflex, Madopark Quick, Rocaltrol, Oralovite, Kalcidon, Zopiklon, Cosmofer, Tenormin, Simvastatin Ranbaxy, Lanzo, Lergigan, Emla, and Aranesp were selected and in the narrative, the active ingredients should not be included as the information had not been provided by the reporter. Time from first dose to onset was populated for epoetin zeta. The frequency of the second therapy of epoetin zeta was structured as twice per week (previously structured as once per two weeks) and three times a day (previously structured as once in three days). Action taken with suspect drug was populated in the structured field. Dosage form fields for Glucose B. Braun, Nutriflex, Madopark Quick, Rocaltrol, Oralovite, Kalcidon, Zopiklon, Cosmofer, Tenormin, Simvastatin Ranbaxy, Lanzo, Lergigan, Emla, and epoetin zeta were populated. Data entry correction was also made in the therapy dates of epoetin zeta and concomitant drug Glucose B. Braun. Second therapy end date of epoetin zeta was changed to 01-Mar-2012 (previously reported as 01-Mar-2011). Second therapy end date of Glucose B. Braun was changed to 18-Nov-2011 (previously reported as 19-Nov-2011).

Case Comment: Overall case causality: Possible Potential efficacy issue, but consider extent and etiology of underlying anemia. Overall case causality (Follow-up 19 Oct 2012): Possible No change in assessment Overall case causality (Follow-up 22 March 2013): Possible No change in assessment

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-MAR-2012	Haematocrit	0.26, Unknown	0.46 0.35
2	01-MAR-2012	Haemoglobin	85 g/l	153 117
3	01-MAR-2012	Mean cell haemoglobin	29 pg	33 27
4	01-MAR-2012	Mean cell haemoglobin concentration	323 g/l	360 320

Mfr. Control Number: 1430483

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
5	01-MAR-2012	Mean cell volume	91, FL	98 82
6	01-MAR-2012	Platelet count	402 x10 9/l	390 160
7	01-MAR-2012	Red blood cell count	2.9 x10 12/l	5.2 3.9
8	01-MAR-2012	White blood cell count	12.6 x10 9/l	8.8 3.5

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	10000 IU, Freq: 1 Week: Interval: 1; Subcutaneous	Low Hb (Haemoglobin decreased)	30-MAR-2011 / 10-NOV-2011; 226 days
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #2	4000 IU, Monday plus Friday in conjustion with dilaysis; Freq: 2 Week: Interval: 1; Subcutaneous	Low Hb (Haemoglobin decreased)	02-DEC-2011 / 01-MAR-2012; 91 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#2) EMLA /00675501/ (LIDOCAINE, PRILOCAINE) Transdermal patch ; 24-DEC-2011 / Unknown

#6) LERGIGAN /00033002/ (PROMETHAZINE HYDROCHLORIDE) Tablet ; 06-APR-2009 / Unknown

#7) MADOPARK QUICK (BENSERAZIDE HYDROCHLORIDE, LEVODOPA) Tablet ; 06-APR-2009 / Unknown

#8) NUTRIFLEX /07393601/ (ACETIC ACID, ALANINE, AMINO ACIDS NOS, ARGININE, ASPARTIC ACID, CALCIUM, CHLORIDE, GLUCOSE, GLUTAMIC ACID, GLYCINE, HISTIDINE, ISOLEUCINE, LEUCINE, LYSINE, MAGNESIUM, METHIONINE, PHENYLALANINE, PHOSPHORUS, POTASSIUM, PROLINE, SERINE, SODIUM, THREONINE, TRYPTOPHAN, L-, VALINE) Emulsion for infusion ; 17-NOV-2011 / 20-NOV-2011

#9) ORALOVITE (ASCORBIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) Tablet ; 06-APR-2009 / Unknown

#10) ROCALTROL (CALCITRIOL) Capsule ; 06-APR-2009 / Unknown

#11) SIMVASTATIN RANBAXY (SIMVASTATIN) Tablet ; 06-APR-2009 / Unknown

#12) TENORMIN (ATENOLOL) Tablet ; 06-APR-2009 / Unknown

#13) ZOPIKLON (ZOPICLONE) Tablet ; 06-APR-2009 / Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobaco usage were not reported. The patient was not exposed to any other erythropoietin-stimulating agent (ESA); however it was also reported that the patient received Aranesp 40 mcg (darbepoetin alfa; subcutaneous) from 06-Apr-2009 to 19-Aug-2010. Follow up information received on 14-Mar-2013 from the physician. Follow up report was created to reflect new information regarding patient's medical history. The patient was exposed to other erythropoietin-stimulating agents (ESA) Aranesp and Eprex (1000 E; route of administration not reported) from 19-Aug-2010 until

Mfr. Control Number: 1430483

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	30-Mar-2011. Race/Ethnicity: Caucasian.	
Unknown	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
Unknown	Past Drug Event	EPREX (EPREX); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	04	APR	1930	83	Female	84.70 kg	28	AUG	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Heart insufficiency decompensated [Cardiac failure]
Thromboembolic events [Embolism]
Cardiogenic shock [Cardiogenic shock]

Case Description: This is a serious Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia. This report describes case of fatal
asystole.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☒ PATIENT DIED Date: 12-SEP-2013
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 48 IU/Kg/w (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 25-AUG-2010 / Unknown

19. THERAPY DURATION
#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ACTRAPHANE (INSULIN HUMAN, INSULIN HUMAN INJECTION,
#2) ACETYLSALICYLIC ACID (ACETYLSALICYLIC ACID) Tablet ; Unknown
#3) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCC
#4) CELEBREX (CELECOXIB) Capsule ; Unknown
#5) DEKRISTOL (COLECALCIFEROL) ; Unknown
#6) DIOVAN (VALSARTAN) Tablet ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown		()

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2104804

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-JUL-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case from a physician (ref: Ge-048-0016) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta, subcutaneous; dose, frequency and batch number not reported) for renal anaemia. Medical history and concomitant medications were not reported. On an unknown date, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced asystole. Treatment for the event and action taken with the suspect drug was not reported. On 12-Sep-2013, the patient died. Cause of death was asystole. It was not reported if an autopsy was performed. The reporter's causality assessment for the event of fatal asystole in relation to epoetin zeta was not related. It was reported that the cause for this arrhythmic event included preexisting cardiac diseases like hypertensive cardiomyopathy with diastolic dysfunction and repeated congestive cardiac decompensations. 20-Feb-2014: Follow-up information was received from the same reporter. Follow-up report was created to reflect new information obtained regarding patient details, medical history, past drug, suspect drug, adverse event and laboratory tests. Patient details were updated. Heart insufficiency decompensated was added as an adverse event. This case describes an 83-year-old female patient (weight: 80 kg, height: 146 cm). Risks factors included obesity before 2009. Medical history included hyperlipidemia before 2009, diabetes mellitus in 2006 and hypertension in 2000. The patient received Aranesp for an unknown indication without any thromboembolic event during treatment. On 25-Aug-2010, the patient started treatment with epoetin zeta (once a week, batch number not available). On 28-Aug-2013, the patient was hospitalized due to dyspnea, decompensated heart insufficiency. On 29-Aug-2013 at 06:43, glomerular filtration rate was 28.8 ml/min (greater than 66), sodium was 143 mmol/l (135-145), potassium was 3.8 mmol/l (3.5-5.1), calcium was 2.2 mmol/l (2.0-2.6), urea was 168 mg/dl (less than 50), creatinine was 1.70 mg/dl (less than 0.9), glucose was 205 mg/dl (55-110), CK was 582 U/l (less than 170) and CK-MB 61 U/l (less than 22). On the same day of 29-Aug-2013 at 06:43, laboratory values showed elevated Troponin T high sensitive of 2.600 ng/ml (less than 0.014), NSTEMI was suspected. Other cause was reported to be renal insufficiency. On 30-Aug-2013 at 06:43, glomerular filtration rate was 25.3 ml/min, leukocyte was 10620/mcl (3500-9800), erythrocyte was 3.2/pl (4.1-5.1), hemoglobin was 9.1 g/dl (12-16), hematocrit was 29.8% (36-48), MCV was 93.4 fl (80-96), MCH was 28.4 pg/Ery (28-33), MCHC was 30.4 g/dl (32-36), thrombocyte was 334/nl (140-360), sodium was 143 mmol/l, potassium was 3.6 mmol/l, calcium was 2.3 mmol/l, urea was 188 mg/dl, creatinine was 1.90 mg/dl, CK was 204 U/l, CK-MB was 26 U/l and Troponin T high sensitive was 2.700 ng/ml. On the same day of 30-Aug-2013 at 06:55, POCT revealed BE of 4.1 mmol/L (reference value not reported), glucose of 181 mg/dl (74-106), ionized calcium of 1.17 mmol/l (1.12-1.32), COHb of 1.5%, cHCO3 of 29.5 mmol/l (21-28), HHb of 4.7% (1-5), potassium of 4.0 mmol/l (3.5-4.5), lactate of 0.9 mmol/l (0.4-2.2), metHb 1.1% (less than 1), sodium 145 mmol/l (138-148), O2Hb of 92.7% (95-99), pCO2 of 51.6 mmHg (35-45), pH of 7.376 (7.35-7.45), pO2 of 70.6 mmHg (80-100), O2 95.2% (95-98), and tHb 9.9 g/dl (11.7-16.1). On 31-Aug-2013 at 07:10, POCT revealed BE of 5.8 mmol/L, glucose of 124 mg/dl, ionized calcium of 1.19 mmol/l, COHb of 1.6%, cHCO3 of 30.6 mmol/l, HHb of 6.6%, potassium of 4.5 mmol/l (3.5-4.5), lactate of 0.7 mmol/l, metHb 1.1%, sodium 145 mmol/l, O2Hb of 91.7%, pCO2 of 47.5 mmHg, pH of 7.423, pO2 of 63.3 mmHg, O2 94.2%, and tHb 9.2 g/dl. On 31-Aug-2013 at 08:01, glomerular filtration rate was 26.9 ml/min, leukocyte was 9260/mcl, erythrocyte was 3.0/pl, hemoglobin was 8.6 g/dl, hematocrit was 28.4%, MCV was 94.4 fl, MCH was 28.6 pg/Ery, MCHC was 30.3 g/dl, thrombocyte was 331/nl, GOT was 39 U/l (10-35), sodium was 144 mmol/l, potassium was 3.7 mmol/l, calcium was 2.2 mmol/l, creatinine was 1.80 mg/dl, glucose was 112 ng/ml, CK was 106 U/l, LDH was 452 U/l (lessthan 250), magnesium was 0.96 mmol/l (0.7-1.1) and Troponin T high sensitive was 3.710 ng/ml. On 01-Sep-2013 at 08:02, glomerular filtration rate was 30.0 ml/min, leukocyte was 10260/mcl, erythrocyte was 2.9/pl, hemoglobin was 8.3 g/dl, hematocrit was 27.6%, MCV was 94.8 fl, MCH was 28.5 pg/Ery, MCHC was 30.1 g/dl, thrombocyte was 343/nl, Qiuck was 103% (greater than 70), INR was 0.98 (less than 1.3), PTT was 35 sec (less than or equal to 40), sodium was 148 mmol/l, potassium was 4.0 mmol/l, calcium was 2.3 mmol/l, creatinine was 1.64 mg/dl, glucose was 123 ng/ml, magnesium was 0.98 mmol/l and Troponin T high sensitive was 4.240 ng/ml. On 02-Sep-2013 at 10.01, glomerular filtration rate was 17.6 ml/min, leukocyte was 12740/mcl, erythrocyte was 2.8.0/pl, hemoglobin was 8.4 g/dl, hematocrit was 26.3%, MCV was 91.3 fl, MCH was 29.2 pg/Ery, MCHC was 31.9 g/dl, thrombocyte was 344/nl, GOT was 8 U/l , GPT was 22 U/l (10-35), GGT was 31 U/l (less than 40), AP was 55 U/l (35-105), total bilirubin 0.3 mg/dl (less than 1.1), sodium was 144 mmol/l, potassium was 3.9 mmol/l, calcium was 2.5 mmol/l, urea was 239 mg/dl, creatinine was 2.60 mg/dl, ferritin 189 g/dl (15-400), CK was 105 U/l, LDH was 543 U/l (less than 250), Troponin T high sensitive was 3.320 ng/ml, vitamin B12 was 448 ng/l (191-663) and folic acid was 8.2 mcg/l (3.1-17.5). The event was improved by diuretic and antihypertensive (dose and route of administration not reported) treatment while no treatment/intervention was given for elevated Troponin T levels. Action taken with the suspect drug was not reported. On 05-Sep-2013, the patient recovered from the event of heart insufficiency decompensated and was discharged from the hospital. It was reported that the last dose prior to the event was reported as 06-Sep-2013. The reporter’s causality assessment for the event of heart insufficiency decompensated in relation to epoetin zeta was not related. According to the investigator, elevated troponin values were often seen in CKD patients in routine controls due to the reduced renal function and that they had no other signs or symptoms of myocardial ischemia than the elevated troponin level. Based on the investigator, this was not an acute event rather than elevated troponin due to reduced renal function. 07-May-2014: Follow up report was received from the reporter. Follow up report was created to reflect additional information regarding suspect drug, medical history and adverse event. Thromboembolic events were added as an adverse reaction. Dose of Retacrit was 48 IU/kg/week with frequency of once a week. Medical history also included diabetic nephropathy in Jun 2010 that led to renal failure. On an unknown date, the patient experienced thromboembolic events. Action taken with the suspect drug and treatment for the event was not reported. Outcome of thromboembolic events was not reported. The reporter's causality assessment between the event of thromboembolic events and Retacrit was not reported. Hyperlipidaemia, hypertension, and diabetes mellitus type 2 were also considered as risk factors. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number, date of expiry, and previous

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

exposure of patient to other biosimilars. 23-Jun-2014: Follow-up information received from the same reporter. Follow-up report was created to reflect additional information regarding patient details, past drug therapy, concomitant medications, adverse event, and reporter's causality assessment. Adverse event of fatal asystole was changed to fatal cardiogenic shock. Patient's weight was updated to 84.7 kg. Dose of Aranesp was 20 mcg/week. Batch number of Retacrit was not available. The patient was not exposed to other biosimilars only to Aranesp until Aug 2010. Concomitant medications included Aspirin Protect Tablet (acetylsalicylic acid; 100 mg, 0-1-0), Plavix film-tablet (clopidogrel; 75 mg, 1-0-0), Nebilet tablet (nebivolol; 5 mg, 1/2-0-0), valsartan (80 mg, 1-0-1 and 1-0-0), Hct tablet (hydrochlorothiazide; 12.5 mg, 1-0-0), Torem tablet (torasemid; 10 mg, 2-1-0 and 1-1-0), spironolacton tablet (50 mg, 1/2-0-0), amlodipin tablet (5 mg, 1-0-0 and 10 mg, 1/2-0-0-0), Simvahexal filmtablet (simvastin; 20 mg, 0-0-1), allopurinol tablet (100 mg and 300 mg, 0-0-1), L-thyroxin (100 mcg, 1-0-0), Nexium (esomeprazole; 20mg, 0-0-1), prednisolon tablet (5mg, 1-0-0), Dekristol 20,000 I.E. (once a week, dose not reported), Belok Zoc (1-0-0, dose not reported), ASS (100 mg, 0-1-0), Zopiclon (7.5 mg, 0-0-0-1), Actraphane (40 mg-0-20 mg-0), Simva (20 mg, 1-0-0), simvastatin Krewel filmtablet (20 mg, 0-0-1-0), Godamed 100 TAH tablet (1-0-0-0, dose not reported), Euthyrox tablet (100 mcg, 1-0-0-0), torasemid AL tablet (10 mg, 1-1-0-0), Diovan filmtablet (80 mg, 1/2-0-0-0), Celebrex hard capsule (100 mg, 1-0-0-0), and oxazepam tablet (dose not reported); routes of administration not reported, all given for unknown indications. On 13-Aug-2013, laboratory data were as follows: HCT 35.9 % (standard range: 37.0-54.0), Hb 11.4 g/dl (12.0-18.0), potassium 4.9 mmol/L (3.5-5.0), cholesterol 249 mg/dl (up to 200), LDH 445 U/l (up to 480), CK 120 U/l (<190 U/l), CRP 2.3 mg/l (<5.0), and LDL-cholesterol 148 mg/dl (<180 (100) mg/dl). On 12-Sep-2013, the patient was found at home with bradycardia, loss of consciousness, and asystolia and experienced cardiogenic shock. On the same day, patient was hospitalized and received resuscitation without success. Action taken with suspect drug was not reported. 20 The patient died on 12-Sep-2013. Cause of death was changed to cardiogenic shock. It was unknown if an autopsy was performed. The reporter's causality assessment between the event of fatal cardiogenic shock and Retacrit was unlikely. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product Retacrit: batch number. 03-Jul-2014: Translation of the German text from the discharge letter was received. Follow-up report was created to reflect information obtained regarding patient details, medical history, adverse event, and laboratory tests. Medical history also included metabolic syndrome described as type II diabetes mellitus (insulin), morbid obesity, HLP, HU and arterial hypertension. On an unknown date, the patient had nephrectomy on the left, for nephrolithiasis and chronic kidney failure IV with renal anaemia. The patient had tracheostoma for DD: laryngotracheal stenosis in the context of surgery for a nucleus pulposus prolapse of the cerebral vertebra, gonarthrosis on both side and TEP of the right knee on an unknown date. On an unknown date, the patient had hysterectomy, appendectomy, multiple thyroid surgeries 30 years previous, hp-positive peptic ulcer on Aug 2007 and with known cholecystolithiasis. The patient lived at home alone, care level 1, cared for along with daughter and was a wheeled walker. The patient was with ageappropriate overall condition and adipose nutritional status of 80 BMI. Admission as an inpatient took place in consultation with the emergency physician due to severe breathlessness for an hour, dry cough, and had no thoracic symptoms.
Upon admission as an inpatient, the cause of the clinical symptoms appeared to be a decompensated cardiac failure with severe dyspnoea described as CHD with NSTEMI. The patient also had hypertensive heart disease with diastolic dysfunction, Level 2, rec. left cardiac decompensation associated with hypertensive crisis and known mitral valve insufficiency, Level II. The patient was admitted to the intensive care ward. The patient complained of back pain and pain in the area of the lungs. The patient's pupils were isocore, head and neck clinically normal and with dyspnoea at rest. The patient had respiratory breath sounds on both sides with wheezing and buzzing, prolonged expiration, pure and rhythmic heart tones, HR was 108/min, RR was reported as 134/64 mmHg, saturation was 95% with 3 litres oxygen. Abdomen was soft, with pain on palpitation of the right upper abdominal region, no palpable resistance, and normal peristalsis of the bowels. The patient had no pain on percussion of the left renal bed. The patient had age-appropriate motor restrictions. Neurological findings included the patient was oriented, peripheral arteries palpable on both sides and with leg oedema on both sides. The intensive diuretic and antihypertensive treatment recompensated the patient and permitted a transfer to the general care ward. On an unknown date, the patient had ECG that showed sinus rhythm, normal position, ST deviation in T1, AVL, HR: 109/min. Echocardiography done on an unknown date showed poor transthoracic sonographic conditions with limited interpretation capacity, slightly dilated left ventricle, moderately dilated left atrium, slightly dilated right ventricle, slightly dilated right atrium, maintained LV function, questionable hypokinesia basal/posterolateral, significant LV hypertrophy, diastolic malfunction, restriction type, mild degenerative valve changes in the aortic valve, mild aortic valve insufficiency, mitral valve insufficiency II degrees associated with mitral valve sclerosis, no pericardial effusion. Thoracic a.p. x-ray from ward, dated 28-Aug-2013, during the course of cardiac decompensation, the patient had moderate to severe pulmonary venous congestion with globally enlarged heart. The patient also had leaking pleural effusion on both sides. Defined pneumonic infiltrate could not be delimited. Normal width, centrally-positioned mediastinum. Advanced omarthrosis on the left. Blood gas analyses at rest on 28-Aug- 2013, revealed PO2 of 66.1 mmHg, PCO2 of 37.1 mmHG, SO2 of 94.3%, pH of 7.434 and was assessed as nornocapnic normoxia. On 30-Aug-2013, the patient had thoracic a.p. x-ray from ward showed over the course of slight improvement, there is now moderate to severe pulmonary venous congestion with globally enlarged heart with unchanged pleural effusion leaking on both sides. No evidence of pneumonic infiltrate. Laboratory chemical analyses revealed a myocardial infarction. It was reported that they opted for a conservative treatment approach. Over the course of the inpatient stay, the patient’s overall condition continued to improve. The patient was discharged on 05-Sep-2013 to the outpatient follow-up care in significantly better overall condition.

Case Comment: Overall case causality: Not related Noting reporter's assessment, the event is likely due to the patient's preexisting cardiac diseases (hypertensive cardiomyopathy with diastolic dysfunction and repeated congestive cardiac decompensations). - R. Jacot (28 Dec 2013) Follow-up (06 Mar 2014): No change in previous causality assessment. Alternative etiology noted, as well as reported pre-existing and predisposing risk factors. - R. Jacot Follow-up (20 May 2014): Overall case causality: Possible (not reported reporter causality) Hospira causality: Not assessable New information and

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

event noted. No change in assessment for previous events. Thromboembolic events is not assessable.
While labeled, cannot provide event causation without further objective clinical event details and a firm timeline. - R. Jacot Follow-up (02 July 2014): New information noted. The fatal cardiogenic shock is probably not related to Retacrit
as it was previously mentioned that the elevated troponin was due to a chronic condition and not an acute ischemic event. No change in assessment of other events. - N. Gonzales (02 July 2014) Follow-up (10 Jul 2014): New
information pertains to previous hospitalization. No change in causality assessment for the most recent cardiogenic shock. - N. Gonzales

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-SEP-2013	Activated partial thromboplastin time	35 seconds	
2	02-SEP-2013	Alanine aminotransferase	22 IU/l	35 10
3	31-AUG-2013	Aspartate aminotransferase	39 IU/l	35 10
4	02-SEP-2013	Aspartate aminotransferase	8 IU/l	35 10
5	30-AUG-2013	Base excess	4.1 mmol/l	
6	31-AUG-2013	Base excess	5.8 mmol/l	
7	02-SEP-2013	Blood alkaline phosphatase	55 IU/l	105 35
8	30-AUG-2013	Blood bicarbonate	29.5 mmol/l	28 21
9	31-AUG-2013	Blood bicarbonate	30.6 mmol/l	28 21
10	02-SEP-2013	Blood bilirubin	0.3 mg/dl	
11	29-AUG-2013	Blood calcium	2.2 mmol/l	2.6 2.0
12	30-AUG-2013	Blood calcium	2.3 mmol/l	2.6 2.0
13	31-AUG-2013	Blood calcium	2.2 mmol/l	2.6 2.0
14	01-SEP-2013	Blood calcium	2.3 mmol/l	2.6 2.0
15	02-SEP-2013	Blood calcium	2.5 mmol/l	2.6 2.0
16	13-AUG-2013	Blood cholesterol	249 mg/dl	
17	13-AUG-2013	Blood creatine phosphokinase	120 IU/l	
18	29-AUG-2013	Blood creatine phosphokinase	582 IU/l	
19	30-AUG-2013	Blood creatine phosphokinase	204 IU/l	
20	31-AUG-2013	Blood creatine phosphokinase	106 IU/l	
21	02-SEP-2013	Blood creatine phosphokinase	105 IU/l	
22	29-AUG-2013	Blood creatine phosphokinase MB	61 IU/l	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
23	30-AUG-2013	Blood creatine phosphokinase MB	26 IU/l	
24	29-AUG-2013	Blood creatinine	1.70 mg/dl	
25	30-AUG-2013	Blood creatinine	1.90 mg/dl	
26	31-AUG-2013	Blood creatinine	1.80 mg/dl	
27	01-SEP-2013	Blood creatinine	1.64 mg/dl	
28	02-SEP-2013	Blood creatinine	2.60 mg/dl	
29	02-SEP-2013	Blood folate	8.2, MCG/L	17.5 3.1
30	28-AUG-2013	Blood gases	Normocapnic normoxia, Unknown	
31	29-AUG-2013	Blood glucose	205 mg/dl	110 55
32	30-AUG-2013	Blood glucose	181 mg/dl	106 74
33	31-AUG-2013	Blood glucose	124 mg/dl	106 74
34	31-AUG-2013	Blood glucose	112 mg/dl	110 55
35	01-SEP-2013	Blood glucose	123 mg/dl	110 55
36	13-AUG-2013	Blood lactate dehydrogenase	445 IU/l	
37	31-AUG-2013	Blood lactate dehydrogenase	452 IU/l	
38	02-SEP-2013	Blood lactate dehydrogenase	543 IU/l	
39	30-AUG-2013	Blood lactic acid	0.9 mmol/l	2.2 0.4
40	31-AUG-2013	Blood lactic acid	0.7 mmol/l	2.2 0.4
41	31-AUG-2013	Blood magnesium	0.96 mmol/l	1.1 0.7
42	01-SEP-2013	Blood magnesium	0.98 mmol/l	1.1 0.7
43	30-AUG-2013	Blood methaemoglobin	1.1 %	
44	31-AUG-2013	Blood methaemoglobin	1.1 %	
45	13-AUG-2013	Blood potassium	4.9 mmol/l	5.0 3.5
46	29-AUG-2013	Blood potassium	3.8 mmol/l	5.1 3.5
47	30-AUG-2013	Blood potassium	4.0 mmol/l	4.5 3.5
48	30-AUG-2013	Blood potassium	3.6 mmol/l	5.1 3.5

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
49	31-AUG-2013	Blood potassium	3.7 mmol/l	5.1 3.5
50	31-AUG-2013	Blood potassium	4.5 mmol/l	4.5 3.5
51	01-SEP-2013	Blood potassium	4.0 mmol/l	5.1 3.5
52	02-SEP-2013	Blood potassium	3.9 mmol/l	5.1 3.5
53	29-AUG-2013	Blood sodium	143 mmol/l	145 135
54	30-AUG-2013	Blood sodium	143 mmol/l	145 135
55	30-AUG-2013	Blood sodium	145 mmol/l	148 138
56	31-AUG-2013	Blood sodium	145 mmol/l	148 138
57	31-AUG-2013	Blood sodium	144 mmol/l	145 135
58	01-SEP-2013	Blood sodium	148 mmol/l	145 135
59	02-SEP-2013	Blood sodium	144 mmol/l	145 135
60	29-AUG-2013	Blood urea	168 mg/dl	
61	30-AUG-2013	Blood urea	188 mg/dl	
62	02-SEP-2013	Blood urea	239 mg/dl	
63		Body mass index	80, Unknown	
64	13-AUG-2013	C-reactive protein	2.3 mg/l	
65	30-AUG-2013	Calcium ionised	1.17 mmol/l	1.32 1.12
66	31-AUG-2013	Calcium ionised	1.19 mmol/l	1.32 1.12
67	30-AUG-2013	Carboxyhaemoglobin	1.5 %	
68	31-AUG-2013	Carboxyhaemoglobin	1.6 %	
69	28-AUG-2013	Chest X-ray	Defined pneumonic infiltrate not be delimited, Unk	
70	28-AUG-2013	Chest X-ray	With globally enlarged heart,Unknown	
71	28-AUG-2013	Chest X-ray	Normal width, centrally-positioned mediastinum, Un	
72	28-AUG-2013	Chest X-ray	Moderate to severe pulmonary venous congestion, Un	
73	28-AUG-2013	Chest X-ray	Advanced omarthrosis on the left, Unknown	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
74	28-AUG-2013	Chest X-ray	Leaking pleural effusion on both sides, Unknown	
75	30-AUG-2013	Chest X-ray	Moderate to severe pulmonary venous congestion, Un	
76	30-AUG-2013	Chest X-ray	No evidence of pneumonic infiltrate,Unknown	
77	30-AUG-2013	Chest X-ray	With globally enlarged heart, Unknown	
78	30-AUG-2013	Chest X-ray	Unchanged pleural effusion leaking on both sides,U	
79		Echocardiogram	Mitral valve insufficiency II degrees, Unknown	
80		Echocardiogram	Slightly dilated left ventricle,Unknown	
81		Echocardiogram	No pericardial effusion,Unknown	
82		Echocardiogram	With limited interpretation capacity,Unknown	
83		Echocardiogram	Associated with mitral valve sclerosis, Unknown	
84		Echocardiogram	Maintained LV function, Unknown	
85		Echocardiogram	Mild aortic valve insufficiency, Unknown	
86		Echocardiogram	Mild degenerative valve changes in aortic valve,Un	
87		Echocardiogram	Moderately dilated left atrium,Unknown	
88		Echocardiogram	Poor transthoracic sonographic conditions,Unknown	
89		Echocardiogram	Questionable hypokinesia basal/posterolateral,Unk	
90		Echocardiogram	Significant LV hypertrophy, diastolic malfunction,	
91		Echocardiogram	Slightly dilated right atrium,Unknown	
92		Echocardiogram	Slightly dilated right ventricle,Unknown	
93		Electrocardiogram	AVL, HR: 109/min, Unknown	
94		Electrocardiogram	Sinus rhythm, normal position, ST deviation in T1,	
95	02-SEP-2013	Gamma-glutamyltransferase	31 IU/l	
96	29-AUG-2013	Glomerular filtration rate	28.8 ml/min	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
97	30-AUG-2013	Glomerular filtration rate	25.3 ml/min	
98	31-AUG-2013	Glomerular filtration rate	26.9 ml/min	
99	01-SEP-2013	Glomerular filtration rate	30.0 ml/min	
100	02-SEP-2013	Glomerular filtration rate	17.6 ml/min	
101	13-AUG-2013	Haematocrit	35.9 %	54.0 37.0
102	30-AUG-2013	Haematocrit	29.8 %	48 36
103	31-AUG-2013	Haematocrit	28.4 %	48 36
104	01-SEP-2013	Haematocrit	27.6 %	48 36
105	02-SEP-2013	Haematocrit	26.3 %	48 36
106	13-AUG-2013	Haemoglobin	11.4 g/dl	18.0 12.0
107	30-AUG-2013	Haemoglobin	9.1 g/dl	16 12
108	30-AUG-2013	Haemoglobin	4.7 %	5 1
109	30-AUG-2013	Haemoglobin	9.9 g/dl	16.1 11.7
110	31-AUG-2013	Haemoglobin	8.6 g/dl	16 12
111	31-AUG-2013	Haemoglobin	6.6 %	5 1
112	31-AUG-2013	Haemoglobin	9.2 g/dl	16.1 11.7
113	01-SEP-2013	Haemoglobin	8.3 g/dl	16 12
114	02-SEP-2013	Haemoglobin	8.4 g/dl	16 12
115		Heart rate	108/min, Unknown	
116	01-SEP-2013	International normalised ratio	0.98, Unknown	
117	13-AUG-2013	Low density lipoprotein	148 mg/dl	
118	30-AUG-2013	Mean cell haemoglobin	28.4 pg/Ery, Unknown	33 28
119	31-AUG-2013	Mean cell haemoglobin	28.6 pg/Ery, Unknown	33 28
120	01-SEP-2013	Mean cell haemoglobin	28.5 pg/Ery, Unknown	33 28
121	02-SEP-2013	Mean cell haemoglobin	29.2 pg/Ery,Unknown	33 28
122	30-AUG-2013	Mean cell haemoglobin concentration	30.4 g/dl	36 32

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
123	31-AUG-2013	Mean cell haemoglobin concentration	30.3 g/dl	36 32
124	01-SEP-2013	Mean cell haemoglobin concentration	30.1 g/dl	36 32
125	02-SEP-2013	Mean cell haemoglobin concentration	31.9 g/dl	36 32
126	30-AUG-2013	Mean cell volume	93.4, FL	96 80
127	31-AUG-2013	Mean cell volume	94.4, FL	96 80
128	01-SEP-2013	Mean cell volume	94.8, FL	96 80
129	02-SEP-2013	Mean cell volume	91.3, FL	96 80
130		Neurological examination	Leg oedema on both sides,Unknown	
131		Neurological examination	Oriented, peripheral arteries palpable both sides,	
132		Oxygen saturation	95 %	
133	28-AUG-2013	Oxygen saturation	94.3 %	
134	30-AUG-2013	Oxygen saturation	92.7 %	99 95
135	30-AUG-2013	Oxygen saturation	95.2 %	98 95
136	31-AUG-2013	Oxygen saturation	91.7 %	99 95
137	31-AUG-2013	Oxygen saturation	94.2 %	98 95
138		PCO2	7.423, Unknown	
139	30-AUG-2013	PCO2	51.6 mmHg	45 35
140	31-AUG-2013	PCO2	47.5 mmHg	45 35
141	28-AUG-2013	PO2	66.1 mmHg	
142	30-AUG-2013	PO2	70.6 mmHg	100 80
143	31-AUG-2013	PO2	63.3 mmHg	100 80
144		Physical examination	Respiratory breath sounds on both sides, Unknown	
145		Physical examination	Pure and rhythmic heart tones,Unknown	
146		Physical examination	Pupils isocore, head and neck clinically normal, U	
147		Physical examination	Age-appropriate motor	

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
			restrictions,Unknown	
148		Physical examination	Soft pain palpitation right upper abdomen region,U	
149		Physical examination	No pain on percussion of the left renal bed,Unknow	
150		Physical examination	No palpable resistance normal peristalsis bowels,	
151		Physical examination	With wheezing and buzzing, prolonged expiration, U	
152		Physical examination	Dyspnoea at rest, Unknown	
153	30-AUG-2013	Platelet count	334/nl, Unknown	360 140
154	31-AUG-2013	Platelet count	331/nl, Unknown	360 140
155	01-SEP-2013	Platelet count	343/nl, Unknown	360 140
156	02-SEP-2013	Platelet count	344/nl, Unknown	360 140
157	01-SEP-2013	Prothrombin time	103 %	
158	30-AUG-2013	Red blood cell count	3.2/pl, Unknown	5.1 4.1
159	31-AUG-2013	Red blood cell count	3.0/pl, Unknown	5.1 4.1
160	01-SEP-2013	Red blood cell count	2.9/pl, Unknown	5.1 4.1
161	02-SEP-2013	Red blood cell count	2.8/pl, Unknown	5.1 4.1
162		Respiratory rate	134/64 mmHg	
163	02-SEP-2013	Serum ferritin	189 ng/ml	400 15
164	29-AUG-2013	Troponin T	2.600 ng/ml	
165	30-AUG-2013	Troponin T	2.700 ng/ml	
166	31-AUG-2013	Troponin T	3.710 ng/ml	
167	01-SEP-2013	Troponin T	4.240 ng/ml	
168	02-SEP-2013	Troponin T	3.320 ng/ml	
169	02-SEP-2013	Vitamin B12	448 ng/ml	663 191
170	30-AUG-2013	White blood cell count	10620/mcl, Unknown	9800 3500
171	31-AUG-2013	White blood cell count	9260/mcl, Unknown	9800 3500
172	02-SEP-2013	White blood cell count	10260/mcl, Unknown	9800 3500
173	02-SEP-2013	White blood cell count	12740/mcl, Unknown	9800

Mfr. Control Number: 2104804

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
				3500
174	28-AUG-2013	pH body fluid	7.434, Unknown	
175	30-AUG-2013	pH body fluid	7.376, Unknown	7.45 7.35
176	31-AUG-2013	pH body fluid	7.423, Unknown	7.45 7.35

13. Relevant Tests

Abdomen : No palpable resistance normal peristalsis bowels, Unknown
Abdomen : Soft pain palpitation right upper abdomen region,Unknown
ECG: Sinus rhythm, normal position, ST deviation in T1, Unknown
Echocardiography: Mild degenerative valve changes in aortic valve,Unknown
Echocardiography: Significant LV hypertrophy, diastolic malfunction,Unknown
Neurological findings: Oriented, peripheral arteries palpable both sides, Unknown
Physical examination: Pupils isocore, head and neck clinically normal, Unknown
Pulmonary: With wheezing and buzzing, prolonged expiration, Unknown
Physical examination: Pupils isocore, head and neck clinically normal, Unknown
Thoracic a.p. x-ray: Moderate to severe pulmonary venous congestion,Unknown
Thoracic a.p. x-ray: Normal width, centrally-positioned mediastinum,Unknown
Thoracic a.p. x-ray: Moderate to severe pulmonary venous congestion,Unknown
Thoracic a.p. x-ray: Unchanged pleural effusion leaking on both sides,Unknown

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	48 IU/Kg/week, Freq:1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	25-AUG-2010 / Unknown; Unknown

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) ACTRAPHANE (INSULIN HUMAN, INSULIN HUMAN INJECTION, ISOPHANE) ; Unknown

#3) BELOC-ZOK COMP (HYDROCHLOROTHIAZIDE, METOPROLOL SUCCINATE) ; Unknown

#7) EUTHYROX (LEVOTHYROXINE SODIUM) Tablet ; Unknown

#8) GODAMED (ACETYLSALICYLIC ACID) ; Unknown

#9) HYDROCHLOROTHIAZIDE (HYDROCHLOROTHIAZIDE) Tablet ; Unknown

#10) NEBIVOLOL (NEBIVOLOL) Tablet ; Unknown

#11) ESOMEPRAZOL /01479301/ (ESOMEPRAZOLE) ; Unknown

#12) CLOPIDOGREL (CLOPIDOGREL) Tablet ; Unknown

#13) SIMVA (SIMVASTATIN) ; Unknown

#14) SIMVAHEXAL (SIMVASTATIN) Tablet ; Unknown

#15) TORASEMID AL (TORASEMIDE) Tablet ; Unknown

#16) TORASEMID (TORASEMIDE) ; Unknown

#17) ZOPICLON (ZOPICLONE) ; Unknown

#18) ALLOPURINOL (ALLOPURINOL) Tablet ; Unknown

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#19) AMLODIPIN /00972401/ (AMLODIPINE) Tablet ; Unknown

#20) ASS (ACETYLSALICYLIC ACID) ; Unknown

#21) L-THYROXIN (LEVOTHYROXINE SODIUM) ; Unknown

#22) OXAZEPAM (OXAZEPAM) Tablet ; Unknown

#23) PREDNISOLON /00016201/ (PREDNISOLONE) Tablet ; Unknown

#24) SIMVASTATIN (SIMVASTATIN) Tablet ; Unknown

#25) SPIRONOLACTON (SPIRONOLACTONE) Tablet ; Unknown

#26) VALSARTAN (VALSARTAN) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage and medical history were not reported. On 12-Sep-2013, the patient died. Cause of death was asystole. It was not reported if an autopsy was performed. 20-Feb-2014: Additional information was received from the same reporter. Follow-up report was created to reflect new information obtained regarding medical history. Risks factors included obesity before 2009. Medical history included hyperlipidemia before 2009, diabetes mellitus in 2006 and hypertension in 2000. The patient received Aranesp for an unknown indication. Race/Ethnicity: Caucasian. 07-May-2014: Additional information was received regarding medical history. Diabetes was described as type 2. Medical history also included diabetic nephropathy in Jun 2010 that led to renal failure. 23-Jun-2014: Follow-up information received from the same reporter. Follow-up report was created to reflect additional information regarding past drug therapy. The patient was not exposed to other biosimilars only to Aranesp until Aug 2010. Dose of Aranesp was 20 mcg/week. The patient died on 12-Sep-2013. Cause of death was changed to cardiogenic shock. It was unknown if an autopsy was performed. 03-Jul-2014: Translation of the German text in discharge document was received. Follow-up report was created to reflect information obtained regarding medical history. Medical history also included metabolic syndrome described as type II diabetes mellitus (insulin), morbid obesity, HLP, HU and arterial hypertension. On an unknown date, the patient had nephrectomy on the left, for nephrolithiasis and chronic kidney failure IV with renal anaemia. The patient had tracheostoma for DD: laryngotracheal stenosis in the context of surgery for a nucleus pulposus prolapse of the cerebral vertebra, gonarthrosis on both side and TEP of the right knee on an unknown date, the patient had nephrectomy on the left, for nephrolithiasis and chronic kidney failure IV with renal anaemia.
Unknown		(); The patient had tracheostoma for DD: laryngotracheal stenosis in the context of surgery for a nucleus pulposus prolapse of the cerebral vertebra, gonarthrosis on both side and TEP of the right knee on an unknown date. On an unknown date, the patient had hysterectomy, appendectomy, multiple thyroid surgeries 30 years previous, hp-positive peptic ulcer on Aug 2007 and with known cholecystolithiasis. The patient lived at home alone, care level 1, cared for along with daughter and was a wheeled walker.
Unknown to Ongoing	Relevant Med History	Kidney failure chronic (Chronic kidney disease);
Unknown to Ongoing	Relevant Med History In 2006	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
Unknown to Ongoing	Relevant Med History	Diabetic nephropathy (Diabetic nephropathy);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Gonarthrosis (Osteoarthritis);
Unknown to Ongoing	Relevant Med History Before 2009	Hyperlipidemia (Hyperlipidaemia);
Unknown to Ongoing	Relevant Med History In 2000	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Renal anaemia (Nephrogenic anaemia);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown	Relevant Med History	Appendectomy (Appendicectomy);
Unknown	Relevant Med History	Cholecystolithiasis (Cholelithiasis);
Unknown	Relevant Med History Aug 2007	Peptic ulcer helicobacter (Peptic ulcer helicobacter);
Unknown	Relevant Med History	Hyperuricemia (Hyperuricaemia);
Unknown	Relevant Med History	Hysterectomy (Hysterectomy);
Unknown	Relevant Med History	Laryngeal stenosis (Laryngeal stenosis);
Unknown	Relevant Med History	Tracheal stenosis (Tracheal stenosis);
Unknown	Relevant Med History 30 years previous	Thyroid operation (Thyroid operation);
Unknown	Relevant Med History on the left	Nephrectomy (Nephrectomy);
Unknown	Relevant Med History	Nephrolithiasis (Nephrolithiasis);
Unknown	Relevant Med History	Surgery herniated nucleus pulposus (Intervertebral disc operation);
Unknown	Relevant Med History	Knee operation (Knee operation);
Unknown	Relevant Med History	Tracheostomy (Tracheostomy);
Unknown	Relevant Med History Risk Factor: Before 2009	Morbid obesity (Obesity);
Unknown	Relevant Med History	Walking aid user (Walking aid user);
26-JUN-2009 to 25-AUG-2010	Past Drug Event	ARANESP (ARANESP); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1960	58 Years	Female	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

This is a Non-Interventional Study report from Protocol Study ID EPOE-09-11. This is a Non-Interventional Study report with non-serious event(s) only.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
From/To Dates | Type of History / Notes | Description
Unknown

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2119610

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-MAY-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of lack of efficacy.
This non-serious case from an investigator (ref: Ge-097-0016) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta; subcutaneous, dose, frequency, and batch number not reported) for renal anaemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced lack of efficacy. Treatment, action taken with the suspect drug and outcome of the adverse event were not reported. The reporter's causality assessment between the event of lack of efficacy and epoetin zeta was not reported. The following information has been requested from the reporter for identification and raceability of the biosimilar product Retacrit: dosage administered, batch number and expiry date and previous exposure to other biosimilars.

Follow-up (06May2019): This is a Non-Interventional Study follow-up report from Protocol Study ID EPOE-09-11.
The female patient was approximately 58 years old.

The reporter's assessment of the causal relationship of the reported event with the suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

Case Comment: Overall case causality: Possible Labeled event but cannot provide a more definitive assessment without objective clinical event details, pertinent laboratory results, medical history and concomitant medications. - N. Gonzales (14 Jan 2014)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1963	56 Years	Female	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lack of efficacy [Drug ineffective]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.
This is a Non-Interventional Study report from Protocol Study ID EPOE-09-11.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

18. THERAPY DATES(from/to)
#1) Unknown

19. THERAPY DURATION
#1) Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
☐ YES ☐ NO ☒ NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
From/To Dates | Type of History / Notes | Description
Unknown

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2119625

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-MAY-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a Non-Interventional Study report with non-serious event(s) only.
This is a Hospira-sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of lack of efficacy.
This non-serious case from an investigator (ref: Ge-097-0016) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta; subcutaneous, dose, frequency, and batch number not reported) for renal anaemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta and experienced lack of efficacy. Treatment, action taken with the suspect drug and outcome of the adverse event were not reported. The reporter's causality assessment between the event of lack of efficacy and epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: dosage administered, batch number and expiry date and previous exposure to other biosimilars.

Follow-up (06May2019): This is a Non-Interventional Study follow-up report from Protocol Study ID EPOE-09-11.
Patient' was a 56-year-old female.

The reporter's assessment of the causal relationship of the reported event with the suspect product was not provided at the time of this report. Since no determination has been received, the case is managed based on the company causality assessment.

Case Comment: Based on the available information there is a reasonable possibility that the drug contributed to occurrence of the event.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GREECE	19	APR	1926	88 Years	Male	69.00 kg	14	MAY	2014

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Anaemia [Anaemia]
Lack of efficacy [Drug ineffective]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a Non-Interventional Study, protocol EPOE-09-11, in regards to subject Gr-017-0020.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☒ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☒ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 434.76 IU/kg, 3 in 1 week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 14-FEB-2014 / 01-JUN-2014	#1) 108 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NORVASC (AMLODIPINE BESILATE) ; 2003 / Unknown
#2) SINTROM (ACENOCOUMAROL) ; 2003 / Unknown
#3) OLARTAN (OLMESARTAN MEDOXOMIL) ; 2003 / Unknown
#4) FEROFOLIC (FERROUS SULFATE, FOLIC ACID) ; 2013 / Unknown
#5) LASIX (FUROSEMIDE) ; 2003 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertensive nephropathy (Hypertensive nephropathy)
APR-2013 to Ongoing	Relevant Med History	Renal failure (Renal failure)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2362260

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-JUL-2016

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This report describes a case of lack of efficacy. This non-serious case from an investigator describes an 88-year-old male patient (weight: 69 kg, height: 172 cm) who received Retacrit (epoetin zeta, 434.78 IU/kg/week, subcutaneous, 3 in 1 week) for renal anaemia on 14Feb2014. Medical history included hypertensive nephropathy which led to renal failure diagnosed in Apr2013. The patient was not on dialysis. The patient was treated with an erythropoiesis-stimulating agent (ESA) before treatment with Retacrit: Eprex (epoetin alfa, 434.78 IU/kg/week) for an unknown indication on 18Nov2013. Concomitant medications were not reported. On 14-Feb-2014, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced lack of efficacy. Treatment for the adverse event and action taken with epoetin zeta were not reported. Outcome of the adverse event was unknown at the time of the report. The reporter's causality assessment of the event of lack of efficacy in relation to epoetin zeta was not reported. Risk factors included atrial fibrillation, hypertension, diabetes type 2.
11-Jun-2014: Corrected report was created to change the overall causality.

Follow-up (13Jul2016): This is a follow-up report from a Non-Interventional Study, protocol EPOE-09-11, in regards to subject Gr-017-0020. New information reported by a physician included: The patient was hospitalized due to anemia (hemoglobin: 6.0 g/dl) unknown etiology. Patient's height and weight added/updated. New medical history included hypothyroidism. New lab data (14May2014) included: NEU 82.8%, LYMPH 8.6%, EOS 0.1%, LYMPH 0.52 x10^3/mcl, RBC 2.87x10^6/mcl, Hg 6 g/dl, HCT 19.4%, MCV 67.45 fl, MCH 20.8 pg, MCHC 30.8 g/dl, RDW 21.8%. Concomitant drugs included amlodipine (NORVASC) at 5 mg daily for hypertension, acenocoumarol (SINTROM) at 2 mg daily for atrial fibrillation, olmesartan (OLARTAN) at 20 mg daily for hypertension, ferrus sulfate (FEROFOLIC) at 525 mg daily for anemia and furosemide (LASIX) at 40 mg daily for hypertension. New event: anemia, onset date 16May2014, life-threatening (LT), hospitalization. The patient had received EPREX from 18Nov2013 to 14Feb2014 at 10000 as an erythropeitin-stimulating agent (ESA) and hemoglobin increased from 9.6 g/dl to 10.3 g/dl. The reporter considered that the event anemia was not related to treatment with epoetin zeta.

Follow-up (18Jul2016): During his admission, the subject was investigated for the anemia. There was no obvious cause, apart from renal function deterioration. The subject was discharged, followed up in the outpatient clinic for 2 months. His renal function declined and he started on hemodialysis. The subject received epoetin zeta from 16May2014 to 01Jun2014. The adverse event anemia resolved with sequalae on 01Jun2014.

Follow-up (25Jul2016). The subject received epoetin zeta from 14Feb2014 to 01Jun2014. The adverse event anemia started on 14May2016 and resolved with sequalae on 01Jun2014. The event according to the results was due to renal function deterioration. There was no evidence that the event was due to Retacrit.

Case Comment: The Company considered there was not a reasonable possibility that the reported events, anemia and lack of efficacy were related to the study drug epoetin zeta. The events were most likely related to the progression of disease under study. The Follow-up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	14-MAY-2014	Eosinophil count	0.1 %	10 0.5
2	14-MAY-2014	Haematocrit	19.4 %	52 40
3	14-MAY-2014	Haemoglobin	6 g/dl	18 14
4	14-MAY-2014	Lymphocyte count	0.52x10^3/ul	3.6 1.5
5	14-MAY-2014	Lymphocyte count	8.6 %	51 20
6	14-MAY-2014	Mean cell haemoglobin	20.8 pg	32 27
7	14-MAY-2014	Mean cell haemoglobin concentration	30.8 g/dl	35 32
8	14-MAY-2014	Mean cell volume	67.45 fL	99 80
9	14-MAY-2014	Neutrophil count	82.8 %	75 45
10	14-MAY-2014	Red blood cell count	2.87x10^6/ul	6.3 4.2

Mfr. Control Number: 2362260

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
11	14-MAY-2014	Red cell distribution width	21.8 %	14.5 11.5

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2003 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation);
2010 to Ongoing	Relevant Med History	Type 2 diabetes mellitus (Type 2 diabetes mellitus);
2003 to Ongoing	Relevant Med History	Hypertension (Hypertension);
18-NOV-2013 to 14-FEB-2014	Past Drug Event	EPOETIN ALFA (EPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)
2013 to Ongoing	Relevant Med History	Hypothyroidism (Hypothyroidism);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	ITALY	25	MAY	1944	72 Years	Male	95.00 kg	10	NOV	2016	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

TIA [Transient ischaemic attack]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a report from a contactable physician from the non-interventional study, protocol EPOE-09-11, regarding subject 1160042.

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 IU, 2x/week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Nephrogenic anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 13-MAY-2014 / 05-SEP-2016	#1) 847 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) INSULIN (INSULIN HUMAN) ; 1997 / Ongoing
#2) LASIX (FUROSEMIDE) ; Ongoing
#3) NORVASC (AMLODIPINE BESILATE) ; Ongoing
#4) PLAVIX (CLOPIDOGREL BISULFATE) ; 2010 / Ongoing
#5) GABAPENTIN (GABAPENTIN) ; 2010 / Ongoing
#6) ARIXTRA (FONDAPARINUX SODIUM) ; 2010 / Ongoing

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension)
1997 to Ongoing	Relevant Med History	Diabetes (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2017455775

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-JAN-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 72-year-old Caucasian Hispanic or Latino male subject received epoetin zeta (RETACRIT) 4000 IU subcutaneously twice a week from 13May2014 to 05Sep2016 for the study indication of nephrogenic anemia. The subject's medical history was significant for hypertension, diabetes mellitus since 1997, and peripheral arterial occlusive disease since 2010, all ongoing. Concomitantly, the subject was taking insulin human (INSULIN) subcutaneously since 1997 for diabetes mellitus, furosemide (LASIX) orally for hypertension, amlodipine besilate (NORVASC) orally for hypertension, clopidogrel bisulfate (PLAVIX) orally since 2010 for peripheral arterial disease, gabapentin orally since 2010 for peripheral arterial disease, fondaparinux sodium (ARIXTRA) subcutaneously since 2010 for peripheral arterial disease, ferrous sulfate (FERROGRAD) orally for "IRC", epoetin beta (NEORECORMON) subcutaneously since 05Sep2016 for "IRC", and sodium bicarbonate orally for gastric protection, all ongoing. On 10Nov2016, the subject experienced a transient ischemic attack (TIA). A computerized tomogram (CT) cranio on 10Nov2016 showed TIA. The investigator reported that there were no acute infarction or hemorrhagic lesions but chrome vascular damages. Treatment details, if any, were not provided. The subject was considered to have recovered from the event on an unspecified date; recovery date reported as 24h. The event was assessed as non-serious. The investigator considered that the relationship of the event to treatment with study drug and concomitant drugs was unrelated.

Pfizer assessed the event TIA to be serious, medically significant.

Follow-up (26Oct2017): Updates subject data, study drug data, and event resolve data.

Amendment: This follow-up report is being submitted to amend previously reported information: The investigator reported "no acute infarction or hemorrhagic lesions. Chronic vascular damages".

Amendment: This follow-up report is being submitted to amend previously reported information: The case was downgraded to non-serious.

Case Comment: In agreement with the investigator, the Company considered the event Transient ischaemic attack (TIA) is unlikely related to study medication epoetin zeta. The underlying diseases of hypertension, diabetes mellitus and peripheral arterial occlusive disease were considered as contributor factors in the event. The follow up information received does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	10-NOV-2016	Computerised tomogram	TIA	

13. Relevant Tests

CT skull-brain (10NOv2016): reason for test "transient aphasia". Examination performed in emergency with direct scans of 5 mm contiguous from the skull base up to the peak. At present, no acute focal densitometry alterations, or intraparenchymal or extracerebral blood clusters. Conditions compatible with chronic ischemic vascular suffering with homogeneous lipodensity of the supratentorial white substance. Ventricular-cylindrical structures in axis, little expanded in relation to initial atrophy.
Midline in Axis. Calcifications of carotid and vertebral arteries.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) FERROGRAD (FERROUS SULFATE) ; Ongoing

#8) NEORECORMON (EPOETIN BETA) ; 05-SEP-2016 / Ongoing

#9) SODIUM BICARBONATE (SODIUM BICARBONATE) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2010 to Ongoing	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);

TABLE OF CONTENTS

15.3.12.3.2 Treatment-Related Non-Serious Adverse Event (Adverse Drug Reaction) Narratives

Below is the list of treatment-related non-serious adverse events (adverse drug reaction) cases:

Patient ID Number	Adverse Event Reference (AER) Number	MedDRA Preferred Term(s)
Es-024-0023	1818576	Dermatitis allergic
Fr-051-0009	1431731	Dizziness; Headache; Hypertension; Malaise; Nausea; Palpitations
Ge-048-0008	1689755	Malaise; Nightmare
Ge-067-0018	1406283	Breast disorder
Ge-101-0001	1230033	Headache
Ge-142-0006	1023545	Lip swelling; Swollen tongue; Vulvovaginal pruritus
Ge-147-0001	2299509	Pruritus; Rash
Ge-479-0001	2426421	Malaise
Sw-018-0010	2169429	Influenza like illness

This clinical trial report contains narratives printed in a CIOMS format with a “Draft” watermark. This watermark signifies that these narratives were not produced for the submission of individual case safety reports to a regulatory agency. These narratives contain the information available in the safety database as of 27-Aug-2020 and are considered final.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	21	SEP	1937	73 Years	Female	53.00 kg	26	APR	2011

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pruritus of vagina [Vulvovaginal pruritus]
Swelling of lips [Lip swelling]
Swelling of tongue [Swollen tongue]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO II) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of swelling of lips
and tongue and pruritus of vagina.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 40000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 13-APR-2011 / 26-APR-2011

19. THERAPY DURATION
#1) 14 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NEBIVOLOL STADA (NEBIVOLOL HYDROCHLORIDE) Tablet ; Unknown
#2) ASS (ACETYLSALICYLIC ACID) Tablet ; Unknown
#3) ATACAND (CANDESARTAN CILEXETIL) Tablet ; Unknown
#4) BONDRONAT /01304701/ (IBANDRONIC ACID) ; Unknown
#5) FUROSEMIDE (FUROSEMIDE) Tablet ; Unknown
#6) PANTOPRAZOLE (PANTOPRAZOLE) Tablet ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown	Relevant Med History April-2009	Bowen's disease (Bowen's disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1023545

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-JAN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1023545

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This case describes a 73-year old, female patient (ID number not given) who received Retacrit (epoetin zeta) (4000 IU, subcutaneous, twice a week, formulation, batch number not reported) for renal anemia starting on 13-Apr-2011. Medical history was not reported. The patient had no known drug hypersensitivities nor any history of drug dependence. Concomitant medications included Prednison Galen (prednisone) 5mg, 1/2 tablet every two days, taken in the morning; Prograf (tacrolimus) 0.5mg, one capsule taken in the morning; Prograf (tacrolimus) 1mg, one capsule taken in the evening; Vigantoletten 1000 (colecalciferol), one tablet taken in the morning; Bondronat 2mg/2ml vial, dose not reported; Furosemid Basics (furosemide) 40mg tablet, pause; Atacand (candesartan) 16mg tablet; 1/2 tablet in the morning and 1/2 tablet in the evening; Nebivolol Stada 5mg, 1/2 tablet taken in the morning; ASS 100mg protecid taken lifelong, 1 enteric-coated tablet taken in the morning; and Pantoprazol Biomo (pantoprazol) 20mg, one enteric-coated tablet taken in the morning; all routes of administration not reported. The reporter also stated that the patient had not received the suspect drug before. On 13-Apr-2011, the patient began treatment with Retacrit (epoetin zeta). On 26-Apr-2011, the patient experienced swelling of lips and tongue and pruritus of vagina. Treatment was not reported. The suspect drug was discontinued on 26-Apr-2011 and the patient's condition improved on 27-Apr-2011 and was fully recovered. The reporter's assessment between the events of swelling of lips and tongue and pruritus of vagina and Retacrit (epoetin zeta) was possible. 23 Jan 2014: Updates received from the investigator regarding patient details, medical history and adverse event. In the narrative, the active substance names of Prograf, Vigantoletten, Bondronat, and Atacand should not be included as the information were not provided by the reporter. Proprietary Medicinal Product name of Nebivolol Stada was selected. Frequency of epoetin zeta was corrected to twice a week and every two days for prednisone in the structured fields. The dose of Vigantoletten was corrected to 1 DF. Dechallenge details was corrrected to positive. The weight of the patient was reflected in the narrative. The patient initials were updated. The patient's weight was 53 kg. Reference number for this case is Ge-142-0006. The patient underwent kidney transplant on 30-Jan-1997. Medical history included Bowen disease of the skin diagnosed in April-2009 with surgery but no chemotherapy. It was also reported that the patient received erythropoetin alpha (subcutaneous; dose not reported) 1 year before treatment with epoetin zeta for 3 months in 2012 and there were no signs of allergy with erythropoetin alpha. Concomitant medications prednisone and tacrolimus were given for immunosupression. No treatment was given for the adverse events.

Case Comment: Overall Case Causality: Possible Temporally related and labeled event; consider contributory effects of concomitant medications and unreported medical history Follow-up (31 Jan 2014): Updates noted, but these do not merit a change in the previous assessment. - R. Jacot.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	40000 IU, Freq: 2 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	13-APR-2011 / 26-APR-2011; 14 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) PREDNISONE (PREDNISONE) Tablet ; Unknown

#8) PROGRAF (TACROLIMUS) Capsule ; Unknown

#9) VIGANTOLETTEN (COLECALCIFEROL) Tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage, and medical history were not reported. The patient had no known drug hypersensitivities and no history of any drug dependence. 23-Jan-2014: Additional information was received regarding the patient's medical history: The patient underwent kidney transplant on 30-Jan-1997. Medical history included Bowen disease of the skin diagnosed in April-2009 with surgery but no chemotherapy. It was also reported that the patient received erythropoetin alpha (subcutaneous; dose not reported) 1 year before treatment with epoetin zeta for 3 months in 2012 and there were no signs of allergy with erythropoetin alpha.
Unknown 27-Aug-2020 04:21	Relevant Med History	Kidney transplant (Renal transplant);

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
	30-Jan-1997	
Unknown	Relevant Med History	Surgery (Surgery);
Unknown	Past Drug Event	EPOETIN ALFA (EPOETIN ALFA); Drug Indication: Drug use for unknown indication (Product used for unknown indication), Drug Reaction: No adverse event (No adverse event)
	Route= Subcutaneous	

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day	Month	Year				Day	Month	Year	
UNKNOWN	GERMANY	22	APR	1930	81 Years	Male	84.00 kg	07	MAR	2012	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Headache [Headache]

Case Description: This is a Hospira-Sponsored Post authorisation safety cohort observation (PASCO II) of Retacrit (epoetin zeta), from Germany, administered subcutaneously, for the treatment of renal anaemia. This report describes a case of headache.
This case describes an 81-year-old male patient who received Retacrit (epoetin zeta; 12, 000 UI/week, subcutaneous, batch number unknown) fo renal anaemia from 01-Nov-2011 to 07-Mar-2012. The patient had no known history of

(Continued on Additional Information Page)

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG?
☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 12000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☒ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 01-NOV-2011 / 08-MAR-2012

19. THERAPY DURATION
#1) 129 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPIN HEXAL /00972401/ (AMLODIPINE) ; Unknown
#2) BENAZEPRIL (BENAZEPRIL) ; Unknown
#3) DREISACARB (CALCIUM CARBONATE) ; Unknown
#4) FERRLECIT /00345601/ (ASCORBIC ACID, FERRIC SODIUM CITR
#5) FLOSA (PLANTAGO OVATA) ; Unknown
#6) FUROSEMID /00032601/ (FUROSEMIDE) ; Unknown
(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1230033

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
15-MAR-2012

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1230033

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

hypersensitivities or drug dependence. Concomitant medication included furosemide 125 1A pharma (1-0-0-0), amlodipine Hexal (5 mg, 2-0-1-0), Dreisacarb (calcium carbonate; 2-2-0-0), One alpha (vitamin D and analogs; 0.5 mcg, daily at night), Phosphonorm (aluminum chlorhydrate; 1-1-1-0) Omega 3 salmon oil (2-0-1-0), Nephrotans (sodium bicarbonate; 1-2-1-0), benazepril AL (10mg, 1/2-0-1/2-0), metamizol Hexal (as required), moxonidin 1A Pharma (0.3 mg, 1-0-0-1), Flosa Balance sachets (inulin and indian psyllium, dose not reported), magnesium (0-0-1-0), Ferrlecit (sodium ferric gluconate complex in sucrose injection; 62.5 mg, 2 amps weekly as a short infusion); routes of administration not reported, all given for unknown indications. On 01-Nov-2011, the patient began treatment with epoetin zeta. On 07-Mar-2012, the patient complained of headache 2 hours after application. Treatment for the adverse event was not reported. On 08-Mar-2012, epoetin zeta was discontinued. The symptoms of the patient partially improved but still had headache that was less severe. The patient gradually recovered the following 24 hours. On an unknown date, the patient was rechallenged and the reaction reappeared after reintroduction of epoetin zeta. The reporter's causality assessment between the event of headache and epoetin zeta was possible.

Case Comment: Overall case causality: Possible Temporally related event. Consider contributory effects of concomitant conditions and underlying medical conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body height	173 CM	
2		Weight	84 kg	

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # UNK}; Regimen #1	12000 IU, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	01-NOV-2011 / 08-MAR-2012; 129 days

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) FERRLECIT /00345601/ (ASCORBIC ACID, FERRIC SODIUM CITRATE, FERROUS SULFATE, NICOTINAMIDE, RIBOFLAVIN, THIAMINE MONONITRATE) ; Unknown

#7) MAGNESIUM (MAGNESIUM) ; Unknown

#8) METAMIZOL HEXAL (METAMIZOLE SODIUM) ; Unknown

#9) MOXONIDIN (MOXONIDINE) ; Unknown

#10) NEPHROTRANS (SODIUM BICARBONATE) ; Unknown

#11) OMEGA 3 FISH OIL (FISH OIL) ; Unknown

#12) ONE ALPHA (ALFACALCIDOL) ; Unknown

#13) PHOSPHONORM (ALUMINIUM CHLORHYDROXIDE-COMPLEX) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption, tobacco usage, and medical history were not reported. The patient had no history of hypersensitivities and drug dependence.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY		Unk		Unk	Unk	Unk	03	AUG	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

sensation of tension in her breast [Breast disorder]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This case has been migrated from another database into the current safety database for processing follow-up information.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown / 18-MAR-2015	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
From/To Dates | Type of History / Notes | Description
Unknown

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1406283

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-OCT-2018

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 1406283

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report. This is a Non-Interventional Study report for EPOE-09-11 from a contactable physician. This is a Non-Interventional Study report with non-serious event(s) only.
A subject of unspecified age and gender started to receive epoetin zeta (RETACRIT) subcutaneous from an unspecified date to 18Mar2015 at unknown dosage for renal anaemia. The subject medical history was not reported. The concomitant medications were not reported. The subject experienced sensation of tension in her breast (which was initially reported as Voltage sensitive and updated on 19Oct2018) on 03Aug2012. The action taken for epoetin zeta was unknown. The event outcome was unknown. Causality assessed was related to epoetin zeta. No further information provided. Sample not available. Customer response not required.

Case Comment: Based on the available information, the Company considers that a causal relationship between the reported event "sensation of tension in her breast" and suspect drug epoetin zeta cannot be excluded.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	FRANCE	23	AUG	1926	86 Years	Female	70.00 kg	26	JUL	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Headache [Headache]
Hypertension [Hypertension]
Malaise [Malaise]
Palipitation [Palpitations]
Dizziness [Dizziness]
Nausea [Nausea]

Case Description: This is a Hospira-Sponsored Post authorisation safety cohort observation (PASCO II) of Retacrit (epoetin zeta), from France, administered subcutaneously, for the treatment of renal anaemia.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 20000 IU, (Continued on Additional Information Page)

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 26-JUL-2012 / 27-JUL-2012

19. THERAPY DURATION
#1) 2 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLOR (AMLODIPINE BESILATE) Capsule ; Unknown
#2) COZAAR (LOSARTAN POTASSIUM) ; Unknown
#3) LASILIX /00032601/ (FUROSEMIDE) ; Unknown
#4) TEMERIT (NEBIVOLOL HYDROCHLORIDE) ; Unknown
#5) TEMESTA /00273201/ (LORAZEPAM) ; Unknown
#6) EUPANTOL (PANTOPRAZOLE SODIUM SESQUIHYDRATE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1431731

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-FEB-2013

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This report describes a case of palpitations, malaise, headaches and diastolic hypertension. This non-serious case from a physician (reference: FR-051-0009) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta; subcutaneous, dose, frequency and batch number not reported) for renal anaemia on an unknown date. Medical history and concomitant medications were not reported. Shortly after 21-Jun-2012, on an unspecified date, the patient received the first injection with epoetin zeta. Following the first injection, the patient experienced headaches, palpitations, malaise and diastolic hypertension greater than 200, controlled by the patient's son with a blood pressure at home . After two days, the patient felt better. Following this episode, she has not taken the subcutaneus injections of epoetin zeta. The patient did not visit her doctor and was not taking blood because she was at her son's house, who is a biologist. It was during the patient's consultation on 17-Sep-2012, that she spoke to her doctor. The reporter's causality assessment for the events of palpitations, malaise, headaches and diastolic hypertension in relation to epoetin zeta was not reported. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): Batch number, date of expiry, previous exposure to other biosimilars and dosage administered. Follow-up information received on 12-Oct-2012 from the investigator. Follow-up report created to reflect new information regarding the susect drug, patient, adverse events and laboratory tests. The adverse event terms dizziness and nausea were added. The patient had many known drug sensitivities (unspecified). The patient was prescribed with epoetin zeta (10,000 IU, per week) on 21-Jun-2012. On 26-Jul-2012, the dose was increased to 20,000 IU per week. It was also reported that on an unspecified day in August 2012, at the time of the patient's first injection, the patient had a bad reaction described as having dizziness, nausea, headache and hypertension, measured with a tensiometre by the patient's son. The patient's hemoglobin was 9 g/dl, and epoetin zeta therapy was advised to be resumed, however, the patient refused to start epoetin zeta. The reporter was unable to provide the following information regarding the identification and traceability of the biosimilar product: Batch number, date of expiry and previous exposure to other biosimilars. Follow-up information received on 30-Nov-2012 from the investigator. Follow-up report created to reflect new information regarding the patient. Data entry correction was also performed on the form reference type. Form reference type was changed to others (previously reported as regulatory agency). The patient had started dialysis and was under Aranesp, with no side effect. Follow-up information received on 25-Jan-2013 from the investigator. Follow-up report created to reflect new information regarding the suspect drug, patient details, patient's medical history, adverse event, and causality assessment. The reporter was able to provide the following information regarding the identification and traceability of the biosimilar product epoetin zeta: previous exposure to other biosimilars. The patient was an 86-year-old female (weight: 70 kg; height: 160 cm). The patient did not have any history of drug dependence. The patient's history of drug hypersensitivities was unknown. Medical history included chronic renal failure by nephroangiosclerosis, hypertension, hypercholesterolemia and Dupuytren's disease. The patient did not have any previous exposure to other biosimilars. Concomitant medications included Amlor 10 mg (1 cap, once per day), Temerit (5 mg), Lasilix special 500 mg (1/4 cap at morning and lunch), Cozaar 50 mg (1 cap, once per day); all were given for hypertension, Eupanthol 60 mg (1 cap, once per day) for gastro-oesophageal reflux, and Temesta 2.5 mg (1 cap, once per day) for anxiety; all routes of administration were not reported. On 26-Jul-2012, twenty minutes after the first injection with epoetin zeta, the patient experienced palpitations, malaise sensation with headache and hypertension, observed by the patient's son. On 27-Jul-2012, epoetin zeta was discontinued. The patient recovered from the adverse events on 28-Jul-2012. The patient started hemodialysis on 26-Nov-2012. The reporter's causality assessment for the events of palpitations, malaise, headaches and diastolic hypertension in relation to epoetin zeta was changed to possible. Received English translation of the cover letter on 05-Feb-2013. Follow-up report created to reflect new information regarding patient details and treatment medication. The patient's date of birth was reported. The dose of Aranesp was reported as 80 mcg per week.

Case Comment: Overall case causality: Not assessable Cannot provide causation of events without further objective clinical event details, medical history and concomitant medications. Overall case causality (Follow-up 26 Oct 2012): Not assessable New reported adverse events are likewise not assessable without further objective clinical event details. Follow-up (21 Dec 2012): New patient details noted. No change in causality assessment - N. Gonzales (21 Dec 2012 Follow-up (03 Feb 2013): Overall case and company causality: Possible New information noted. Causality changed to possible due to close temporal relationship with time of administration. Still consider possible contributory effects from underlying medical conditions. - N. Gonzales (03 Feb 2013) Follow-up (13 February 2013): Overall case and company causality: Possible No change in assessment. - R. Jacot (13 February 2013)

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Diastolic hypertension	Greater than 200, Unknown	
2		Haemoglobin	9 g/dl	

14-19. SUSPECT DRUG(S) continued

Mfr. Control Number: 1431731

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection; Regimen #1	20000 IU, Freq: 1 Week; Interval: 1; Subcutaneous	Renal anaemia (Nephrogenic anaemia)	26-JUL-2012 / 27-JUL-2012; 2 days

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, tobacco usage and medical history were not reported. Follow-up information received on 12-Oct-2012 from the investigator. The patient had many known drug sensitivities. Follow-up information received on 25-Jan-2013 from the investigator. The patient did not have any history of drug dependence. The patient's history of drug hypersensitivities was unknown. The patient did not have any previous exposure to other biosimilars. Medical history included chronic renal failure by nephroangiosclerosis, hypertension, hypercholesterolemia and Dupuytren's disease.
Unknown to Ongoing	Relevant Med History	Hypertension (Hypertension);
Unknown to Ongoing	Relevant Med History	Nephroangiosclerosis (Nephroangiosclerosis);
Unknown	Relevant Med History	Dupuytren's contracture (Dupuytren's contracture);
Unknown	Relevant Med History	Hypercholesterolemia (Hypercholesterolaemia);
Unknown	Relevant Med History	Drug hypersensitivity (Drug hypersensitivity);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GERMANY			1932	80 Years	Male	79.50 kg		DEC	2012

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Indisposition [Malaise]
Nightmare [Nightmare]

Case Description: POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

This is a Hospira-Sponsored Post-Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta) administered

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Exp.Dt. 01-AUG-2014}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 8000 IU, Freq: 1 Week: Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 19-DEC-2011 / 08-JAN-2013

19. THERAPY DURATION
#1) 387 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) AMLODIPIN 1 A PHARMA (AMLODIPINE BESILATE) Tablet ; Unknown
#2) ASS AL (ACETYLSALICYLIC ACID) Tablet ; Unknown
#3) DEKRISTOL (COLECALCIFEROL) ; Unknown
#4) RAMILICH (RAMIPRIL) Tablet ; Unknown
#5) RAMIPLUS STADA (HYDROCHLOROTHIAZIDE, RAMIPRIL) Tablet ; Unknown
#6) TOREM /01036502/ (TORASEMIDE SODIUM) Tablet ; Unknown

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1689755

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-SEP-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

subcutaneously for the treatment of renal anaemia (PASCO II). This report from Germany describes a case of nightmare and indisposition. This non-serious case from an investigator (reference: Ge-048-0008) describes an 80-years-old male subject (weight: 79.5 kg and height: 162 cm) who received Retacrit (epoetin zeta, 8000 IE, subcutaneous, weekly; Batch number: 2E272F; expiration date: 01Aug2014) for renal anemia from 19-Dec-2011 until 08-Jan-2013. The subject previously received epoetin zeta, had no known drug hypersensitivities, and no history of drug dependence. Concomitant medications included Ramilich 5 mg tablet (0-0-1-0), Ramiplus Stada 5 mg/25 mg tablet (1-0-0-0), Torem 10 tablet (1-0-0-0), ASS AL 100 tablet (1-0-0-0), amlodipin 1A Pharma 10 mg tablet (0-0-1/2-0), Dekristol 20000 I.E softgels (1x/week), metoprolol succinate 47.5 prolonged-release tablet (1-0-0-0) and Tramagit 100 mg (if required), all doses not reported, for unknown indications. On 19-Dec-2011, the subject started treatment with epoetin zeta. On an unknown date reported as end of December 2012, the subject reported nightmare and indisposition for 2-3 nights following epoetin zeta administration. However, it was also reported that duration of adverse event was approximately 2-3 weeks. Therapy end date of epoetin zeta was reported to be 08-Jan-2013; however, it was also reported that epoetin zeta was discontinued on 18-Jan-2013. On an unknown date on beginning of January 2013, the subject fully recovered from the adverse events. It was reported that the subject was rechallenged and the reaction reappeared after reintroduction. Dechallenge was positive. The subject had no previous exposure to other biosimilars. Batch number of epoetin zeta was 2E272F. Treatment with epoetin zeta was discontinued on 08-Jan-2013 (previously reported as 18-Jan-2013).

The reporter's causality assessment for the events of nightmare and indisposition in relation to epoetin zeta was possible.

Follow-up (25Sep2019): New information from the investigator included: Subject's year of birth and dechallenge result (positive).

No follow-up attempts are needed. No further information is expected.

Case Comment: Based on the compatible temporal association with positive rechallenge result, the reported events nightmare and indisposition are possibly related to suspect drug epoetin zeta.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) TRAMAGIT (TRAMADOL HYDROCHLORIDE) ; Unknown

#8) METOPROLOL SUCCINATE (METOPROLOL SUCCINATE) Prolonged-release tablet ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event	Epoetin Zeta (EPOETIN ZETA); Drug Indication: Drug use for unknown indication (Product used for unknown indication)

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SPAIN	13	AUG	1938	74 Years	Female	80.00 kg	13	FEB	2013

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Skin allergic [Dermatitis allergic]

Case Description: This case has been migrated from another database into the current safety database for processing follow-up information. As a consequence of this migration, the follow-up report may indicate in the appropriate field that it is an initial report.

POST-AUTHORISATION SAFETY COHORT OBSERVATION OF RETACRIT (EPOETIN ZETA) ADMINISTERED SUBCUTANEOUSLY FOR THE TREATMENT OF RENAL ANAEMIA (PASCO II)

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection {Lot # 2J30652; Exp.Dt. 01-JAN-2015}

20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 6000 IU, weekly

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)
#1) 13-FEB-2013 / 17-JUL-2013

19. THERAPY DURATION
#1) 155 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) EUCREAS (METFORMIN HYDROCHLORIDE, VILDAGLIPTIN) ; Unknown
#2) KALPRESS PLUS (HYDROCHLOROTHIAZIDE, VALSARTAN) ; Unknown
#3) ATORVASTATIN (ATORVASTATIN) ; Unknown
#4) OMEPRAZOL (OMEPRAZOLE) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
From/To Dates | Type of History / Notes | Description
Unknown

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
1818576

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-AUG-2020

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a report from Pfizer Sponsored Non-Interventional Study and post authorization safety study for Protocol EPOE-09-11. This is a non-interventional clinical study case reporting non-serious events only.
This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Spain, administered subcutaneously for the treatment of renal anaemia. This report describes a case of allergy to Retacrit.
This non-serious case from an investigator (reference: 024-0023) describes a patient (age and gender not reported) who received Retacrit (epoetin zeta; subcutaneous; dose, frequency, batch number and formulation not reported) for renal anaemia on an unknown date. Medical history and concomitant medications were not reported. On an unknown date, the patient received epoetin zeta. On an unknown date, the patient experienced allergy to Retacrit. Action taken with epoetin zeta, treatment and outcome of the adverse event were not reported. It was reported that the reason for withdrawal of the patient from the study is the allergy to Retacrit. It was reported that the patient did not complete the study and was withdrawn on 17Jul2013 It was reported that the reason for withdrawal of the patient from the study is the allergy to Retacrit. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit (epoetin zeta): Dose administered, batch number, date of expiry, and previous exposure to other biosimilars. 01Nov2013: Additional information was received from the same reporter. Follow up report was created to reflect new information regarding patient details, adverse event, medical history, concomitant medications, suspect drug, and reporter's causality assessment. The adverse event term was replaced with 'skin allergic'. This case involves a 75-year-old female patient (weight: 80 kg and height: 164 cm). The patient did not have previous exposure to any biosimilar products. Concomitant medications included atorvastatin (1 day), Eucreas (2 times a day), Kalpress plus (1 day), and omeprazol (1 day); doses not reported, routes of administration oral, and given for unknown indications. On 13Feb2013, the patient received Retacrit (6000 ui, once a week, batch number 2J30652). On the same day, the patient experienced skin allergic. Outcome of the adverse event was recovering at the time of the report. However, it was also reported that the event skin allergic ended on 17Jul2013. The reporter's causality assessment for the event of skin allergic in relation to Retacrit was probable

Follow-up (16Jul2019): New information reported includes: updated subject's age to 74 years old. Additionally, study drug action taken in response to event has been corrected to withdrawn temporarily (reported as withdrawn).

This follow-up report is being submitted to amend previously reported information: to amend action taken to "withdrawn temporarily" from "not applicable".

Amendment: This follow-up report is being submitted to amend previously reported information: "For dermatology" deleted in narrative. Indication considered as renal anaemia instead of dermatology.

Case Comment: Overall case causality: Related Hospira causality: Probable Temporally related and labeled event, but cannot provide a definitive causation without confirmatory laboratory test results, if any. - N. Gonzales (06 Sep 2013) Follow-up:
Overall case causality: Probable No change in previous company assessment. - N. Gonzales (10 Nov 2013)
The follow-up information received does not alter the previous company clinical evaluation.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	SWEDEN		Unk		74 Years	Male	83.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Influenza like symptoms [Influenza like illness]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Sweden, administered subcutaneously for the treatment of renal anaemia. This report describes a case of influenza like
symptoms. This case from an investigator (reference: Sw-018-0010) describes a 74-year-old male patient (weight: 83 kg and height: 167 cm) who received Retacrit (epoetin zeta, 4,000 E/week, subcutaneous; batch number unknown) for

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG?
☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 4000 E Freq: 1 Week, Interval: 1

16. ROUTE(S) OF ADMINISTRATION
#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 10-JUN-2013 / 21-JAN-2014

19. THERAPY DURATION
#1) 226 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History GFR 17	Chronic renal failure (Chronic kidney disease)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2169429

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-FEB-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

anemia from 10-Jun-2013 to 21-Jan-2014. The patient had no history of drug dependence. Concomitant medications were not reported. On 10-Jun-2013, the patient started treatment with epoetin zeta. On an unknown date, reported as one day after the Retacrit injection, the patient got influenza like symptoms which lasted for 2-3 days. Treatment for the adverse events was not reported. Treatment with epoetin zeta was discontinued on 21-Jan-2014. It was reported that the patient thought the event were caused by Retacrit and withdrew his consent due to the ADR. Outcome of influenza like symptoms was recovered on an unknown date. The reporter's causality assessment for the events of influenza like symptoms in relation to Retacrit was possible. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. 25-Feb-2014: Follow up information was received from the investigator. Follow up report was created to reflect additional information regarding medical history and concomitant medications. The reporter was able to provide the following information for identification and traceability of the biosimilar product Retacrit: previous exposure of patient to other biosimilars. Data entry correction was made to reflect that this case is non-serious. Medical history included chronic renal failure since 2008, now GFR 17. The patient did not have any previous exposure to other biosimilar products. There were no concomitant medications.

Case Comment: Overall case causality: Possible While seemingly temporally related and with a positive dechallenge, cannot give a more definitive assessment without further objective clinical event details and a more detailed medical history. - R. Jacot (10 Feb 2014) Follow-up (10 Mar 2014): No change in previous company assessment. - R. Jacot

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Allergies, alcohol consumption, and tobacco usage were not reported. The patient had no history of drug dependence. 25-Feb-2014: Additional information was received from the investigator regarding medical history. Medical history included chronic renal failure since 2008, now GFR 17. The patient did not have any previous exposure to other biosimilar products.

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY	01	MAR	1934	79 Years	Male	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Feeling unwell [Malaise]

Case Description: This is a Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta), from Germany, administered subcutaneously for the treatment of renal anaemia. This report describes a case of feeling unwell.
This non-serious case from an investigator (ref: Ge-479-0001) describes a case of a 79-year-old male patient (height: 176 cm; dry weight: 74 kg) who received Retacrit (epoetin zeta; 25 IU/kg/week, dose also reported as 2000 IU/kg/week;

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 25 IU/kg, Freq: 1 week, Interval:1	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Renal anaemia (Nephrogenic anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 09-OCT-2013 / Unknown	#1) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ASS (ACETYLSALICYLIC ACID) ; Unknown
#2) BISOPROLOL (BISOPROLOL) ; 01-JAN-2012 / Unknown
#3) FEBUXOSTAT (FEBUXOSTAT) ; 01-JAN-2012 / Unknown
#4) LISINOPRIL (LISINOPRIL) ; 01-JAN-2012 / Unknown
#5) TORASEMID (TORASEMIDE) ; 01-JAN-2012 / Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown		()
Unknown to Ongoing	Relevant Med History	Confused (Confusional state)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2426421

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JAN-2014

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

subcutaneous; batch number not reported) for renal anemia since 09-Oct-2013. The patient had no known drug hypersensitivities or drug dependence. Medical history included nephrocalcinosis leading to renal failure, colitis ulcerosa for more than 35 years, colectomy in 1980 which was also reported as s/p partial colon resection for benign tumour replaced with artificial anus, gout, restless legs syndrome, hyperuricaemia, presbyacusia on both sides, nephropathy associated with kidney stones in childhood, and iron deficiency anaemia. It was reported that renal failure was first diagnosed on 14-May-2012 and the patient was not on dialysis. Concomitant medications included bisoprolol (2 x 2.5 mg, daily, total daily dose of 5 mg, oral), lisinopril (2 x 5 mg, daily, total daily dose of 10 mg, oral), and torasemid (5 mg, daily, oral) for hypertension; ASS (100 mg, once a day; route of administration not reported) for atherosclerosis; and febuxostat (40 mg, daily, dose also reported as 1 x 40; route of administration not reported) for gout. On 09-Oct-2013 the patient started treatment with epoetin zeta. On 10-Nov-2013, the patient experienced TIA. On 18-Nov-2013, the patient signed the inform consent for the study. Since on an unknown date, the patient was feeling unwell after Retacrit injection. Treatment for the adverse event was not reported. On 20-Nov-2013, the patient was withdrawn from the study due to the adverse event. Outcome of the event of feeling unwell was not reported. The reporter's causality assessment of the event of feeling unwell in relation to epoetin zeta was not reported. Risk factors included peripheral arterial disease described as atherosclerosis, hypertension, and elderly. The following information has been requested from the reporter for identification and traceability of the biosimilar product Retacrit: batch number and previous exposure of patient to other biosimilars. 07-Jul-2014: Corrected report was created to reflect information regarding the adverse event, concurrent condition, and to reflect the reporter's causality assessment. It was reported that the adverse event occurred two times after treatment. It was also reported that the patient was sometimes a bit confused and the investigator does not see a relation to Retacrit.

Case Comment: Overall case causality: Possible Hospira causality: Not assessable Feeling of unwell is a general statement. Cannot provide a definite causality assessment wiithout objective clinical event details. Since patient has numerous significant comorbidities in the medical history, consider also possibility that event is due to underlying medical condition. - N. Gonzales (05 Jul 2014) Follow-up (08 Jul 2014): Overall case causality: Not assessable Feeling of unwell remains not assessable due to limited information. - N. Gonzales (08 Jul 2014)

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown		(); Alcohol consumption and tobacco usage were not reported. The patient had no known drug hypersensitivities or drug dependence. Medical history included nephrocalcinosis leading to renal failure, colitis ulcerosa for more than 35 years, colectomy in 1980 which was also reported as s/p partial colon resection for benign tumour replaced with artificial anus, gout, restless legs syndrome, hyperuricaemia, presbyacusia on both sides, nephropathy associated with kidney stones in childhood, and iron deficiency anaemia. It was reported that renal failure was first diagnosed on 14-May-2012 and the patient was not on dialysis. Risk factors included peripheral arterial disease described as atherosclerosis, hypertension, and elderly. 07-Jul-2014: Corrected report was created to add a bit confused as a concurrent condition.
Unknown to Ongoing	Relevant Med History	Colitis ulcerative (Colitis ulcerative);
Unknown to Ongoing	Relevant Med History	Gout (Gout);
Unknown to Ongoing	Relevant Med History	Hyperuricaemia (Hyperuricaemia);
Unknown to Ongoing	Relevant Med History	Iron deficiency anaemia (Iron deficiency anaemia);
Unknown to Ongoing	Relevant Med History	Nephrocalcinosis (Nephrocalcinosis);
Unknown to Ongoing	Relevant Med History	Nephropathy (Nephropathy);
Unknown to Ongoing	Relevant Med History	Presbyacusia (Presbyacusis);
Unknown to Ongoing	Relevant Med History	Renal failure (Renal failure);
Unknown to Ongoing	Relevant Med History	Restless legs syndrome (Restless legs syndrome);

Mfr. Control Number: 2426421

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Artificial anus (Enterostomy);
Unknown	Relevant Med History	Benign neoplasm (Benign neoplasm);
Unknown	Relevant Med History	Kidney stones (Nephrolithiasis);
Unknown	Relevant Med History	Colectomy partial (Colectomy);
Unknown	Relevant Med History	TIA (Transient ischaemic attack);
Unknown	Relevant Med History	Elderly (Elderly);
Unknown	Relevant Med History	Hypertension (Hypertension);
Unknown	Relevant Med History	Peripheral arterial disease (Peripheral arterial occlusive disease);

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
UNKNOWN	GERMANY			1945	68 Years	Female	113.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pruritus [Pruritus]
Red efflorescences on the skin [Rash]

Case Description: This is an initial report from a Non-Interventional study of Hospira-Sponsored Post Authorisation Safety Cohort Observation (PASCO) of Retacrit (epoetin zeta). This non-serious case from a physician (ref: Ge-147-0001) describes a 68-year-old female patient (weight: 113 kg; height: 160 cm) who received epoetin zeta (EPOETIN ZETA RETACRIT; 4000 per week, subcutaneous, strength 4000; batch number unknown) for anaemia from 02-Jul-2013 until 19-Dec-2013.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Epoetin Zeta (EPOETIN ZETA) Solution for injection

20. DID REACTION ABATE AFTER STOPPING DRUG? ☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 4000 per week	#1) Subcutaneous

17. INDICATION(S) FOR USE
#1) Anaemia (Anaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 02-JUL-2013 / 19-DEC-2013	#1) 171 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) APIDRA (INSULIN GLULISINE) ; Unknown
#2) ASS (ACETYLSALICYLIC ACID) Tablet ; Unknown
#3) CANDIO-HERMAL (NYSTATIN) Cream ; Unknown
#4) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHE
#5) LANTUS (INSULIN GLARGINE) ; Unknown
#6) PANTOPRAZOL 1A PHARMA (PANTOPRAZOLE SODIUM SESQUIHYD

(Continued on Additional Information Page)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Diabetes mellitus (Diabetes mellitus)
Unknown to Ongoing	Relevant Med History	Candida albicans infection (Candida infection)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
235 E42nd Street
New York, NY 10017 UNITED STATES
Phone: 212 733 4552

26. REMARKS

24b. MFR CONTROL NO.
2299509

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-MAR-2019

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-AUG-2020

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient had no known drug hypersensitivities and no history of drug dependence. The patient did not receive the suspect drug before. Medical history included no eosinophilia, infection with Candida albicans, and known diabetes mellitus. Concomitant medications included (Acetylsalicylic Acid)ASS 100 mg enteric-coated tablets (1/2-0-0-0), Valsartan (PROVAS) 80 mg film-coated tablets (1-0-1-0), Torasemide (UNAT) 10 tablets (2-2-0-0, on HD free days),Pantoprazole Sodium Sesquihydrate (PANTOPRAZOL) 1A PHARMA 40 mg enteric-coated tablets (0-0-1-0), metoclopramide hydrochloride (PASPERTIN) drops (30-30-30-0), Insulin Glulisine (APIDRA) 100 E/ml cylindrical ampules (after blood sugar; dose not reported), Insulin Glargine (LANTUS) 100 E/ml cylindrical ampules (0-0-0-4), Ascorbic Acid, Biotin, Calcium Pantothenate, Folic Acid, Nicotinamide, Pyridoxine Hydrochloride, Riboflavin, Thiamine Hydrochloride (DREISAVIT) N film-coated tablets (0-0-1-0), Moliform Premium soft super (as necessary; dose not reported), and Nystatin (CANDIO HERMAL) cream (4 x tbl. bds; dose not reported) (routes of administration for all not reported); all for unknown indications. On 02-Jul-2013, the patient started treatment with epoetin zeta. On an unknown date, the patient experienced red efflorescences on the skin and pruritus. There were no relevant tests or laboratory tests date. Treatment for the adverse events was not reported. Last dose of epoetin zeta was administered on 19-Dec-2013 and was discontinued on 26-Dec-2013. It was reported that the skin was normal. The reporter's causality assessment of the eventa of pruritus and red efflorescences on the skin in relation to epoetin zeta was possible. The following information has been requested from the reporter for identification and traceability of the biosimilar product epoetin zeta: previous exposure of patient to other biosimilars. Upon the follow up on 14Mar2019, patient information regarding date birth was received form the investigator. The action taken was Permanently Withdrawn. The events outcome was recovered.

Follow-up (14Mar2019): New information received from the investigator includes: patient information.

Case Comment: Based on the information provided, the possible contribution of suspect drug epoetin zeta to the events red efflorescence on the skin and pruritus cannot be excluded.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4) DREISAVIT N (ASCORBIC ACID, BIOTIN, CALCIUM PANTOTHENATE, FOLIC ACID, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, RIBOFLAVIN, THIAMINE HYDROCHLORIDE) Tablet ; Unknown

#6) PANTOPRAZOL 1A PHARMA (PANTOPRAZOLE SODIUM SESQUIHYDRATE) Tablet ; Unknown

#7) PASPERTIN /00041902/ (METOCLOPRAMIDE HYDROCHLORIDE) ; Unknown

#8) PROVAS /01319601/ (VALSARTAN) Tablet ; Unknown

#9) UNAT /01036501/ (TORASEMIDE) Tablet ; Unknown

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-034016 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-001-B001	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-01-17 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2011-04-03 Outcome: recovered	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Arteriosclerosis Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Apr-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 9N116DO, SC 3000 IU weekly since 2011-Jan-17 for renal anemia. On 2011-Apr-03 the patient was hospitalised due to shunt occlusion. A shunt revision was scheduled on 2011-Apr-04. The patient's medical history included arteriosclerosis. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 report was received from the hospital physician on 2011-Apr-27. The patient was hospitalised from 2011-Apr-04 to 2011-Apr-15. The new shunt was inserted surgically and the patient was discharged in good condition.
DE-STADA-055922 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-001-B001	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-01-17 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2012-09-03 Outcome: fatal	Cerebral haemorrhage / epoetin zeta: unlikely related	Cerebral haemorrhage / epoetin zeta: not assessable	Cerebral haemorrhage / epoetin zeta: listed	Diabetic nephropathy Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jan-15 and on 2012-Jan-16. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 6000 IU weekly since 2011-Jan-17 for renal anemia. The patient was hospitalised with cerebral haemorrhage from 2012-Sep-03 to 2012-Sep-12 and was then transferred to the rehabilitation unit. The patient died on 2012-Sep-30 due to multiple organ failure. Medical history included hypertension and diabetic nephropathy. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-034016 (same patient)
DE-STADA-036065 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B002	unknown	Male	SILAPO INN: epoetin zeta Start: 2011-01-19 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Acute myocardial infarction Onset: 2011-05-09 Outcome: not recovered	Acute myocardial infarction / epoetin zeta: not assessable	Acute myocardial infarction / epoetin zeta: not assessable	Acute myocardial infarction / epoetin zeta: listed	Cerebrovascular insufficiency Coronary arterial stent insertion Diabetic nephropathy Diabetic retinopathy Diabetic vascular disorder Endocarditis Hyperlipidaemia Hyperparathyroidism secondary Hypertension In-stent coronary artery restenosis Mitral valve replacement Nephrogenic anaemia Osteoarthritis Peripheral arterial occlusive disease Renal failure Skin necrosis Skin ulcer Staphylococcal infection Thrombectomy Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Jun-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A patient (subject number: 001-011) received SILAPO (INN: epoetin zeta) for renal anemia. In 2011-May the patient experienced a non ST segment elevation myocardial infarction. Follow-up #1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Jun-09 and 2011-Jun-6. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient, has been receiving SILAPO (INN: epoetin zeta) 9000 IU SC from 2011-Jan-19. Last SILAPO administration prior to the event was on 2011-May-09. On 2011-May-09 the patient experienced a non ST segment elevation myocardial infarction which required hospitalisation. Special treatment of the event included implantation of a bare metal stent and two drug eluting stents. On 2011-May-19 the patient was discharged. The outcome of the event was reported to be ongoing. The patient's medical history included renal insufficiency, renal anaemia due to diabetic nephropathy, diabetic angiopathy, diabetic retinopathy, type II diabetes mellitus, hypertension arterial, cerebrovascular insufficiency, peripheral arterial occlusive disease, thrombectomy of arteria femoralis, wet necrosis, MRSA positiv, arthrosis, ulcus cruris of lower legs, hyperparathyroidismus secondary, hyperlipidaemia, mitral valve replacement after mitral valve endocarditis, stent insertion, in-stent restenosis. According to the reporter the causal relationship between SILAPO and event was not assessable.
DE-STADA-043688 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B005	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-01-20 End: 2011-12-08 Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2011-12-09 Outcome: fatal	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Aortic valve repair Arteriosclerosis Cerebrovascular insufficiency Coronary artery disease Endocarditis Gastrointestinal haemorrhage Haemorrhagic diathesis Hepatitis C Hyperfibrinogenaemia Hypertension Myocardial infarction Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure chronic Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1F22H1U03-2013, SC 10000 IU weekly since 2011-Jan-20 for renal anemia. On 2011-Dec-09 the patient developed lung embolism and was hospitalised. She died the same day. Medical history included end stage renal insufficiency. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 report was received from a physician on 2012-Feb-23. The cause of death was septic shock with multiple organ failure. Patient's medical history included arteriosclerosis, coronary heart disease, myocardial infarction in May 2004, cerebrovascular insufficiency, peripheral artery occlusive disease, diabetes mellitus type 2, hypertension, chronic hepatitis C, gastrointestinal bleedings, mitral valve endocarditis in Mar 2009, aortic valve repair in June 2004, allergic diathesis and hyperfibrinogenemia.
DE-STADA-038784 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B012	unknown	Female	SILAPO INN: epoetin zeta Start: 2011-01-18 End: not stated Dosage: 1 x 4000 IU per every 1 Day Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-07-19 Outcome: recovered	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Arteriosclerosis Hypertension Hyperthyroidism Mixed hyperlipidaemia Nephrogenic anaemia Osteoporosis Restless legs syndrome Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Sep-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient, has been receiving SILAPO (INN: epoetin zeta) 4000 IU from 2011-Jan-18 for renal anaemia. On 2011-Jul-19 the patient experienced myocardial infarction which required hospitalisation. Subsequently the patient recovered and was discharged on 2011-Jul-25. The last SILAPO administration prior to the event was on 2011-Jul-19. According to the reporter, the causal relationship between SILAPO and event was not assessable.
DE-STADA-033507 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-001-B013	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-01-18 End: 2011-03-13 Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2011-03-13 Outcome: fatal	Cerebral haemorrhage / epoetin zeta: not assessable	Cerebral haemorrhage / epoetin zeta: not assessable	Cerebral haemorrhage / epoetin zeta: listed	Glomerulonephritis Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Osteoporosis Peripheral arterial occlusive disease Renal failure chronic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Mar-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 15000 IU weekly since 2010-Jan-18 for renal anemia. On 2011-Mar-13 the patient was hospitalised with medulla oblongata bleeding. The patient died on 2011-Mar-14. The patient's medical history included hypertension. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 information was received from the hospital physician on 2011-Apr-15. On 2011-Mar-13 the patient developed hemiparesis during dialysis. The patient was tetraparetic on admission and a magentic resonance imaging revealed a medullary bleeding. In the course of dialysis the patient developed acute respiratory paralysis and cardiac arrest and died on 2011-Mar-14. Medical history included also peripheral arterial occlusive disease, chronic renal insufficiency, glomerulonephritis, sec. hyperparathyroidism, renal anaemia and osteoporosis.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-071821 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-001-B018	60 to 69	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2011-01-20 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2013-06-06 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Coronary artery disease Hypertension Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jan-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 12000 IU subcutaneously weekly since 2011-Jan-20 for renal anemia. On 2013-Jun-06 the patient was hospitalised with increasing dyspnoea and chest pressure. An unstable angina pectoris was diagnosed. The patient underwent conservative therapy and the event resolved. The patient was discharged on 2013-Jun-26. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Medical history included diabetes mellitus type 2, hypertension and coronary heart disease.
DE-STADA-033866 v3.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B018	80 to 89	Female	ASS 100 INN: acetylsalicylic acid Start: 2003-02-04 End: not stated Dosage: 1 x 100 mg per every 1 Day Dosage text: not stated RoA: unknown SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2011-01-17 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	alfacalcidol INN: alfacalcidol Indication: Product used for unknown indication bisoprolol INN: bisoprolol Indication: Product used for unknown indication calcium INN: calcium Indication: Product used for unknown indication Dekristol INN: cholecalciferol Indication: Product used for unknown indication Dreisavit INN: vitamins nos Indication: Product used for unknown indication Ferrlecit INN: iron Indication: Product used for unknown indication metamizole INN: metamizole Indication: Product used for unknown indication Mirtazelon INN: mirtazapine Indication: Product used for unknown indication Nitrangin INN: glyceryl trinitrate Indication: Product used for unknown indication omeprazole INN: omeprazole Indication: Product used for unknown indication Restex INN: benserazide,levodopa Indication: Product used for unknown indication salbutamol INN: salbutamol Indication: Product used for unknown indication Simvabeta INN: simvastatin Indication: Product used for unknown indication Spiriva INN: tiotropium bromide Indication: Product used for unknown indication tramadol INN: tramadol Indication: Product used for unknown indication	Gastrointestinal haemorrhage Onset: 2011-03-28 Outcome: unknown	Gastrointestinal haemorrhage / acetylsalicylic acid: not related Gastrointestinal haemorrhage / epoetin zeta: not assessable	Gastrointestinal haemorrhage / acetylsalicylic acid: possible related Gastrointestinal haemorrhage / epoetin zeta: not related	Gastrointestinal haemorrhage / acetylsalicylic acid: listed Gastrointestinal haemorrhage / epoetin zeta: not listed	Cerebrovascular insufficiency Cholecystectomy Coronary artery disease Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Normochromic normocytic anaemia Pancreatitis chronic Polycystic liver disease Renal cyst Renal failure chronic Spinal osteoarthritis Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Mar-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta), batch: 9N116D0, SC 9000 IU weekly since 2011-Jan-17 for renal anemia. On 2011-Mar-28 the patient was hospitalised with gastrointestinal bleeding. The outcome of the event was unknown. The patient's medical history included diabetes mellitus. Concomitant medication was ASS 100 (INN: acetylsalicylic acid), Dreisavit (INN: multivitamins), Spiriva (INN: tiotropium bromide), salbutamol, Simvabeta (INN: simvastatin), Nitrangin (INN: glyceryl trinitrate), omeprazole, tramadol, bisoprolol, Restex (INN: levodopa/benserazide), novaminsulfon (synonym for metamizole), Mirtazelon (INN: mirtazapine), calcium acetate, Ferrlecit (INN: iron), Dekristol (INN: cholecalciferol), alfacalcidol. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 was received from the physician on 2011-Apr-05. Investigations revealed duodenal ulcer Forrest 1a and axial hiatus hernia. Results of laboratory investigations were also provided (haemoglobin, haematocrit). The patient's medical history included chronic pancreatitis, liver cysts, renal cysts, condition after cholecystectomy, terminal renal insufficiency, renal anaemia, hyperparathyroidism sec, hypertension arterial, coronary heart disease, cerebrovascular insufficiency, degeneration of spine, macrocytic normochromic anaemia. Follow-up #2 was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Apr-25. This multimorbid patient was hospitalised due to increased infection signs and severe deterioration of general condition. The patient died on 2012-Feb-28 in hospital due to pneumonia. The reporter assessed the causal relationship between death and SILAPO as not related.
DE-STADA-044073 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B019	70 to 79	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2011-01-20 End: not stated Dosage: 1 x 333.33 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-02-07 Outcome: recovered with sequel	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Arrhythmia Arteriosclerosis Cardiac failure Cataract Coronary artery disease Drug hypersensitivity Erysipelas Goitre Hyperlipidaemia Hypertension Hyperuricaemia Myocardial infarction Nephrogenic anaemia Nephrolithiasis Pancreas lipomatosis Parkinson's disease Polyneuropathy Renal failure chronic Tremor Uterine prolapse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta), batch: 1E207F1/02-2013, SC 333.33 IU weekly since 2011-Jan-20 for renal anemia. On 2012-Feb-07 the patient developed dyspnoea and was hospitalised. A lung embolism was diagnosed. The patient recovered with sequelae and was discharged on 2012-Feb-18. Medical history included cardiac insufficiency, erysipelas of right foot, hypertension, coronary heart disease, myocardial infarction in Jan 2000, cardiac dysrhythmia, arteriosclerosis, chronic renal insufficiency, nephrolithiasis, hyperlipidemia, hyperuricemia, struma nodosa, uterus prolaps, parkinson's disease, cataract incipiens, tremor, polyneuropathy, pancreas lipomatosis and clopidogrel allergy. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-033508 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B021	70 to 79	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2011-01-20 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2011-03-13 Outcome: recovered	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Femur fracture Hyperlipidaemia Hypertension Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure Renal hypertension Renal osteodystrophy Staphylococcal infection Urinary tract infection	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Mar-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) SC 2000 IU weekly since 2010-Jan-20 for renal anemia. On 2011-Mar-13 the patient was hospitalised due to suspicion of transient ischemic attack. At the time of report the outcome was unknown. The patient's medical history included insulin-dependent diabetes mellitus type 2. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up information #1 was received from the hospital physician on 2011-Mar-29. The patient was hospitalised on 2011-Mar-13 after a facial paresis during dialysis which was diagnosed as transient ischemic attack. On 2011-Mar-21 the patient was discharged in stable condition. Medical history of the patient included also hypertension, renal insufficiency, renal hypertension, renal osteopathy, hyperlipoproteinemia, MRSA positiv, peripheral arterial occlusive disease, femur fracture and at the time of report urinary tract infection treated with ciprofloxacin.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-043669 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-001-B023	40 to 49	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-19 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Haemorrhagic stroke Onset: 2011-12-19 Outcome: recovered	Haemorrhagic stroke / epoetin zeta: not assessable	Haemorrhagic stroke / epoetin zeta: not assessable	Haemorrhagic stroke / epoetin zeta: listed	Appendicectomy Arteriosclerosis Brain stem infarction Dehydration Dialysis Drug dependence Drug hypersensitivity Hypertension Hyperuricaemia Hysterectomy Lower limb fracture Mental disorder Metabolic syndrome Nephrogenic anaemia Obesity Renal failure chronic Staphylococcal infection Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1E207F1/02-2n13, SC 1000 IU weekly since 2011-Jan-19 for renal anemia. On 2011-Dec-19 the patient developed an hemorrhagic stroke and was hospitalised. The event resolved on 2011-Dec-29 and the patient was discharged. Medical history included chronic renal insufficiency and dependant on dialysis since December 2005, diabetes mellitus type 2, hypertension, metabolic syndrome, adipositas, hyperuricemia, arteriosclerosis, brain infarction on 2011-Nov-04, psychiatric disorder, drug dependence, hysterectomy in 1991, appendectomy, penicillin allergy, chronic MRSA infection since 2007, lower leg fracture in June 2007 and June 2011 and exsiccosis in August 2011. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-033850 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-001-B027	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-20 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Leukoencephalopathy Onset: 2011-03-27 Outcome: recovered	Leukoencephalopathy / epoetin zeta: unknown	Leukoencephalopathy / epoetin zeta: unlikely related	Leukoencephalopathy / epoetin zeta: not listed	Breast cancer female Coronary artery disease Hypertension Myocardial infarction Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Mar-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 9L101M9, SC 1000 IU weekly since 2011-Jan-20 for renal anemia. On 2011-Mar-27 the patient was hospitalised with transient ischaemic attacks with corresponding symptoms. At the time of report the event was ongoing. The patient's medical history included coronary heart disease and myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 information was received from the hospital physician on 2011-Apr-04. The patient was hospitalised with speech disorder. A tomography revealed leukoencephalopathy. The patient was treated and discharged on 2011-Mar-31. No signs of ischaemia or bleeding were detected. Medical history included also hypertension and condition after breast cancer.
DE-STADA-085457 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-003-B001	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-18 End: 2014-04-25 Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2014-04-27 Outcome: not recovered	Deep vein thrombosis / epoetin zeta: possible related	Deep vein thrombosis / epoetin zeta: possible related	Deep vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 5000 IU weekly since 2011-Feb-18 for renal anemia. On 2014-Apr-27 the patient developed deep vein thrombosis of the lower left limb and was hospitalised. The patient received compression stockings and an anticoagulant therapy was initiated with Falithrom (INN: phenprocoumon). The patient was discharged on 2014-May-03. The event was not resolved at the time of report. SILAPO treatment was interrupted on 2014-Apr-25. The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-055105 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-003-B008	50 to 59	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-15 End: 2012-07-20 Dosage: 1 x 2500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-10-14 Outcome: fatal	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia Obesity Peripheral arterial occlusive disease Renal hypertension Toe amputation Type 2 diabetes mellitus Varicose vein	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-18 and on 2012-Dec-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 2500 IU weekly subcutaneously from 2011-Feb-15 to 2012-Jul-20 for renal anemia. Few months after withdrawal of SILAPO, on 2012-Oct-14, the patient developed pulmonary embolism and was hospitalised. Reanimation and lysis therapy was performed but the patient died. Fourteen days prior to the onset of pulmonary embolism the patient underwent surgery and underwent immobilisation before and after surgery. The reporter assessed the causal relationship between event and SILAPO as not assessable. Medical history included varicosis cruris, peripheral arterial occlusive disease, amputation of toe, adipositas, renal hypertension and diabetes mellitus type 2.
DE-STADA-085458 v1.0	Yes Other medical important condition	DE-003-B010	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-05-07 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	ramipril INN: ramipril Indication: Hypertension	Angina unstable Onset: 2014-05-28 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 1000 IU subcutaneously weekly since 2013-May-07 for renal anemia. Since 2014-May-28 the patient suffered from occasionally occurring chest tightness (unstable angina pectoris) which spontaneously disappeared few hours later. The patient's antihypertensive medication (ramipril) was reduced due to hypotension. The event resolved on 2014-Aug-26. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-085410 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-003-B013	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-05-17 End: 2014-06-24 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2014-07-01 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Alcohol use Cirrhosis alcoholic Dialysis Nephrogenic anaemia Oesophageal varices haemorrhage Peritoneal dialysis complication Peritonitis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2013-May-17 for renal anemia. On 2014-Jun-25 the patient was hospitalised for haemorrhagic anemia due to esophageal varices bleeding. On 2014-Jul-01 ECG changes were observed and myocardial infarction was diagnosed. The patient underwent conservative treatment. The patient was discharged on 2014-Jul-07. He died on 2014-Aug-05. The last SILAPO administration before event was on 2014-Jun-24. Patient's medical history included alcohol abuse, ethyltoxic liver cirrhosis since February 2013, dialysis since 2013-Feb-21 and peritoneal dialysis associated peritonitis in July 2014. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-034761 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-005-B001	70 to 79	Male	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Myocardial infarction Onset: 2011-04-29 Outcome: not recovered	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-May-03. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC since 2011-Jan-31 for renal anemia. On 2011-Apr-29 he was hospitalised with myocardial infarction due to angina pectoris. Coronary angiography and stent insertion was performed. At the time of report the event was not resolved. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-May-17. The weekly dose of SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC was 9000 IU. Patient was discharged on 2011-May-05. At the time of report the event was not resolved.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druas only)	Company causality (Suspect druas only)	Listedness (Suspect druas only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-066876 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-005-B015	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2010-12-30 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arteriovenous fistula occlusion Onset: 2013-09-27 Outcome: recovered Arteriovenous fistula occlusion Onset: 2013-10-15 Outcome: recovered Arteriovenous fistula occlusion Onset: 2013-09-30 Outcome: recovered	Arteriovenous fistula occlusion / epoetin zeta: not related	Arteriovenous fistula occlusion / epoetin zeta: not assessable	Arteriovenous fistula occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 9000 IU weekly since 2010-Mar-05 for renal anemia. On 2013-Sep-27 the patient developed a fistula occlusion which was not resolved at the time of report. The causal relationship was not assessed by the reporter. Follow-up information #1 was received on 2013-Oct-14 and on 2013-Oct-17 respectively: The start date of SILAPO was corrected to 2010-Dec-30. The patient was hospitalised on 2013-Sep-27 and a revision of shunt was performed. The fistula occlusion resolved on 2013-Sep-28 and the patient was discharged. The reporter assessed the causal relationship as not related to Silapo. On 2013-Sep-30 the patient again developed fistula occlusion and was hospitalised. The event was treated with implant of venous catheter and the patient was discharged on 2013-Oct-01. The reporter assessed the causal relationship as not related to Silapo. Follow-up information #2 was received on 2013-Nov-19: At the time of report the patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 12000 IU weekly . On 2013-Oct-15 the patient again developed fistula occlusion and was hospitalised. The event was treated with reapplying of AV shunt and the patient was discharged on 2013-Oct-16. The reporter assessed the causal relationship as not related to Silapo.
DE-STADA-171500 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-005-B018	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-03-21 End: 2018-10-08 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Embolism arterial Onset: 2018-09-21 Outcome: fatal Peripheral ischaemia Onset: 2018-09-21 Outcome: fatal	Embolism arterial / epoetin zeta: not related Peripheral ischaemia / epoetin zeta: not related	Embolism arterial / epoetin zeta: not assessable Peripheral ischaemia / epoetin zeta: not assessable	Embolism arterial / epoetin zeta: listed Peripheral ischaemia / epoetin zeta: listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Nov-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Mar-21 for renal anemia. The current SILAPO dose was 6000 IU weekly and batch: 7TO71U7. On 2018-Sep-21 the patient developed thromboembolic occlusion of femoral artery with critical ischaemia of left leg. The patient died due to sepsis at peripheral arterial occlusive disease with ischaemia of left leg on 2018-Oct-08. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-054588 v3.0	Yes Patient died Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-005-B023	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-06-04 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral artery aneurysm Onset: 2012-08-27 Outcome: recovered with sequel Aortic aneurysm rupture Onset: 2013-07-16 Outcome: fatal	Aortic aneurysm rupture / epoetin zeta: not related Peripheral artery aneurysm / epoetin zeta: not related	Aortic aneurysm rupture / epoetin zeta: not related Peripheral artery aneurysm / epoetin zeta: not assessable	Aortic aneurysm rupture / epoetin zeta: not applicable Peripheral artery aneurysm / epoetin zeta: listed	Anaemia Aortic aneurysm Chronic kidney disease Chronic obstructive pulmonary disease Coronary artery disease Gastritis Hiatus hernia Hypertension Mallory-Weiss syndrome Nephrogenic anaemia Secondary hyperthyroidism	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 1M250N1, SC 12000 IU weekly since 2012-Jun-04 for renal anemia. On 2012-Aug-27 he developed partly thrombosed aneurysm of the arteria iliaca. The event involved persistence of significant disability or incapacity. Medical history included Mallory-Weiss syndrome at hiatus hernia with transfusion requiring anemia, antrum gastritis of stomach, chronic renal disease with renal anemia, COPD, abdominal aortic aneurysm without rupture, hypertension, secondary hyperthyroidism and coronary heart disease. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2013-May-29: The patient was hospitalised from 2012-Aug-27 to 2012-Sep-05. The outcome of the event was reported as recovered with sequelae. Follow-up information #2 was received on 2015-Jul-14: The dose of SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) was reduced to 5000 IU weekly. On 2013-Jul-16 the patient developed rupture of abdominal aortic aneurysm and died. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-065668 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-006-B002	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-10-14 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt thrombosis Onset: 2013-08-30 Outcome: recovered	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU intravenously weekly since 2012-Oct-14 for renal anemia. On 2013-Aug-30 the patient developed shunt thrombosis and was hospitalised. The event resolved on 2013-Sep-02 and the patient was discharged on 2013-Sep-05. The reporter assessed the causal relationship between the event and SILAPO as possible related.
DE-STADA-081975 v1.0	Yes Other medical important condition	DE-006-B002	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-10-14 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt thrombosis Onset: 2014-04-23 Outcome: not recovered	Shunt thrombosis / epoetin zeta: not related	Shunt thrombosis / epoetin zeta: not assessable	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Aug-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 4000 IU (the dose was increased from 2000 IU) intravenously weekly since 2012-Oct-14 for renal anemia. On 2014-Apr-23 the patient developed shunt thrombosis. The patient received a dialysis catheter. At the time of report the event was not resolved. The reporter assessed the causal relationship between the event and SILAPO as not related. Cross ref.: DE-STADA-065668 (same patient).
DE-STADA-083996 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-006-B002	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-10-14 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt thrombosis Onset: 2013-12-16 Outcome: recovered	Shunt thrombosis / epoetin zeta: not related	Shunt thrombosis / epoetin zeta: not assessable	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Sep-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU intravenously weekly since 2012-Oct-14 for renal anemia. On 2013-Dec-16 the patient developed shunt thrombosis and was hospitalised. The event resolved on 2013-Dec-18 and the patient was discharged on 2013-Dec-19. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-056337 v3.0	Yes Life threatening	DE-006-B003	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-07-08 End: not stated Dosage: 1 x 4000 IU per every 1 Month Dosage text: not stated RoA: Subcutaneous	Adenuric 80 mg INN: febuxostat Indication: Product used for unknown indication Bicanorm INN: sodium hydrogen carbonate Indication: Product used for unknown indication Dekristol 20000 INN: cholecalciferol Indication: Product used for unknown indication fluvastatin INN: fluvastatin Indication: Product used for unknown indication Vocado 40/10 INN: amlodipine,olmesartan medoxomil Indication: not stated	Shunt thrombosis Onset: 2013-01-22 Outcome: recovered	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jan-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), subcutaneous, 1000 IU weekly since 2012-Jul-08 for renal anemia. On 2013-Jan-18 the application of a shunt was performed. On 2013-Jan-22 the patient developed shunt thrombosis and pancytopenia (leukocytes 2.4/nl, hemoglobin 7.2 g/dl, thrombocytes 44/nl, LDH 322 U/L) which was assessed as life-threatening by the reporter. SILAPO and Adenuric (INN: febuxostat) was immediately stopped. The event was not resolved at the time of report. Concomitant medication was Dekristol 20000 (INN: cholecalciferol), Vocado 40/10 (INN: olmesartan/amlodipine), Bicanorm (INN: sodium hydrogen carbonate), fluvastatin and Adenuric 80 mg (INN: febuxostat). The reporter assessed the causal relationship between the events and SILAPO as possible related. Follow-up information #1 was received on 2013-Jan-31 and 2013-Feb-01: Further laboratory findings showed an error in primary lab control of 2013-Jan-22. The pancytopenia could not be confirmed. Therefore the event was deleted. Hemoglobin and hematocrit were in normal range. Follow-up information #2 was received on 2013-Apr-29: The patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), subcutaneously, 4000 IU once monthly. The shunt thrombosis resolved on 2013-Jan-24. The event did not reappear after SILAPO was reintroduced.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-064570 v5.0	Yes Other medical important condition	DE-006-B003	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-07-08 End: 2013-09 Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2013-08 Outcome: not recovered Anaemia Onset: 2013-08 Outcome: not recovered Haemoglobin decreased Onset: 2013-08 Outcome: not recovered Myelodysplastic syndrome Onset: not stated Outcome: unknown Pancytopenia Onset: not stated Outcome: unknown Refractory anaemia with an excess of blasts Onset: not stated Outcome: unknown Thrombocytopenia Onset: 2013-03-25 Outcome: not recovered	Anaemia / epoetin zeta: not assessable Drug ineffective / epoetin zeta: not assessable Haemoglobin decreased / epoetin zeta: not assessable Myelodysplastic syndrome / epoetin zeta: not related Pancytopenia / epoetin zeta: not assessable Refractory anaemia with an excess of blasts / epoetin zeta: unknown Thrombocytopenia / epoetin zeta: not related	Anaemia / epoetin zeta: not related Drug ineffective / epoetin zeta: unlikely related Haemoglobin decreased / epoetin zeta: not related Myelodysplastic syndrome / epoetin zeta: not related Pancytopenia / epoetin zeta: not related Refractory anaemia with an excess of blasts / epoetin zeta: not related Thrombocytopenia / epoetin zeta: not related	Anaemia / epoetin zeta: listed Drug ineffective / epoetin zeta: listed Haemoglobin decreased / epoetin zeta: listed Myelodysplastic syndrome / epoetin zeta: not listed Pancytopenia / epoetin zeta: not listed Refractory anaemia with an excess of blasts / epoetin zeta: not listed Thrombocytopenia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Aug-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), subcutaneous, 1000 IU weekly since 2012-Jul-08 for renal anemia. Since 2013-Mar-25 a progressive thrombopenia and anemia was detected (thrombocytes 241000 in January 2013 and 93000 in August 2013). Furthermore a HB decrease from 11.5 in January 2013 to 10.1 in August 2013 were observed (lack of drug effect). The events were not resolved at the time of report. The SILAPO therapy was interrupted on 2013-Aug-11. The reporter assessed the causal relationship between the events and SILAPO as not assessable. Cross ref.: DE-STADA-056337 (same patient) Further information was received from the physician on 2013-Aug-13: SILAPO treatment: from 2013-Jan-24 to 2013-Jan-30 discontinuation since 2013-Jan-31: 4000 IU every 8 weeks since 2013-Mar-28: 4000 IU every 4 weeks At the time of report SILAPO was discontinued. Thrombocytes values: 2013-Jan-24:241000/µl End of February 2013:160000/µl End of March 2013:120000/µl End of April 2013:178000/µl End of May 2013:123000/µl End of July 2013: 107000/µl At the time of report:93000/µl Hemoglobin values: 2013-Jan-24:11,9 g/dl End of July 2013: 10,1 g/dl The reporting physician assumed the slight deterioration of hemoglobin values to be caused by the deterioration of renal insufficiency. Administered doses of epoetin zeta were still low and likely to be increased. At the time of report the patient's glomerular filtration rate (GFR) was 12-15 ml/min/1.73m2 and he was uremic. Heparin induced thrombocytopenia caused by heparin treatment due to surgery from 2013-Feb-17 to 2013-Mar-03 was excluded as cause of the events by antibody testing. The patient received allopurinol since 2013-Apr-25 which was withdrawn in July/August 2013 as a possible cause of thrombopenia. Follow-up information #1 was received on 2013-Sep-11: Diagnostic investigation for Pure Red Cell Aplasia (PRCA) were negative. Follow-up information #2 was received on 2013-Sep-26: The patient's condition deteriorated. The hemoglobin value was 8.1 g/dl. Furthermore pancytopenia was reported. SILAPO was discontinued and the patient received darbepoetin. A bone marrow biopsy was scheduled. Follow-up information #3 was received on 2013-Oct-17: A bone marrow biopsy was performed in October 2013 which revealed RAEB 1 (refractory anemia with excess of blasts). Follow-up information #4 was received on 2013-Dec-13: In October 2013 a new myelodysplastic syndrome was diagnosed which was causative for the blood picture changes (thrombocytopenia). The reporter assessed the causal relationship between SILAPO and thrombocytopenia as not related. SILAPO was discontinued in September 2013.
DE-STADA-079985 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B003	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-02-13 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt occlusion Onset: 2014-02-11 Outcome: recovered Pyrexia Onset: 2014-02-11 Outcome: recovered Shunt occlusion Onset: 2014-04-26 Outcome: recovered	Pyrexia / epoetin zeta: unlikely related Shunt occlusion / epoetin zeta: unlikely related	Pyrexia / epoetin zeta: unlikely related Shunt occlusion / epoetin zeta: not assessable	Pyrexia / epoetin zeta: not listed Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jun-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 9000 IU, IV, weekly since 2012-Feb-13 for renal anemia. On 2014-Feb-11 the patient developed shunt occlusion of left upper arm shunt and was hospitalised. postoperatively fever of unknown origin. Thrombectomy and shunt revision was performed. Postoperatively the patient developed fever of unknown origin. The events resolved on 2014-Feb-16. Further information was received the same day (204-Jun-30): The patient again developed shunt occlusion of left upper arm shunt on 2014-Apr-26 and was hospitalised. Thrombectomy was performed and the event resolved on 2014-Apr-28. The reporter assessed the causal relationship to SILAPO as unlikely related.
DE-STADA-069329 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B005	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-02-01 End: not stated Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Haemoglobin decreased Onset: 2013-09-10 Outcome: recovered Gastritis Onset: 2013-09-10 Outcome: recovered Pyrexia Onset: 2013-09-10 Outcome: recovered	Gastritis / epoetin zeta: not related Haemoglobin decreased / epoetin zeta: not related Pyrexia / epoetin zeta: not related	Gastritis / epoetin zeta: not related Haemoglobin decreased / epoetin zeta: unlikely related Pyrexia / epoetin zeta: not related	Gastritis / epoetin zeta: not applicable Haemoglobin decreased / epoetin zeta: listed Pyrexia / epoetin zeta: not applicable	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 5000 IU weekly intravenously since 2011-Feb-01 for renal anemia. On 2013-Sep-10 the patient developed mild gastritis, fever and hemoglobin decrease of unknown origin. The patient was hospitalised and treated with Pantozol (INN: pantoprazole). The events resolved and the patient was discharged on 2013-Sep-16. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-059073 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B016	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-07-10 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2013-02-01 Outcome: recovered	Deep vein thrombosis / epoetin zeta: unlikely related	Deep vein thrombosis / epoetin zeta: possible related	Deep vein thrombosis / epoetin zeta: listed	Chronic hepatitis C Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Apr-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2012-Jul-10 for renal anemia. On 2013-Feb-01 the patient was hospitalised due to deep vein thrombosis of the lower limbs. The patient was treated with phenprocoumon and compression. The event resolved on 2013-Feb-15 and the patient was discharged. The patient's medical history included chronic hepatitis C. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-068391 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-008-B016	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-07-10 End: 2013-09-11 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-10-13 Outcome: fatal Haemorrhage Onset: 2013-10-13 Outcome: fatal Multi-organ failure Onset: 2013-10-13 Outcome: fatal Renal failure acute Onset: 2013-10-13 Outcome: fatal Sepsis Onset: 2013-10-13 Outcome: fatal	Haemorrhage / epoetin zeta: not related Multi-organ failure / epoetin zeta: not related Myocardial infarction / epoetin zeta: not related Renal failure acute / epoetin zeta: not related Sepsis / epoetin zeta: not related	Haemorrhage / epoetin zeta: not related Multi-organ failure / epoetin zeta: not related Myocardial infarction / epoetin zeta: not assessable Renal failure acute / epoetin zeta: not related Sepsis / epoetin zeta: not related	Haemorrhage / epoetin zeta: not listed Multi-organ failure / epoetin zeta: not listed Myocardial infarction / epoetin zeta: listed Renal failure acute / epoetin zeta: not listed Sepsis / epoetin zeta: not listed	Chronic hepatitis C Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU subcutaneously weekly since 2012-Jul-10 for renal anemia. On 2013-Oct-13 the patient developed non-ST-segment elevation myocardial infarction, complicative bleeding, acute renal failure and multi organ failure at sepsis. The patient was hospitalised and a coronary stent implant, anticoagulation and antibiosis therapy was performed. The patient died on 2013-Oct-22. SILAPO therapy was interrupted on 2013-Sep-11. Patient's medical history included chronic hepatitis C. The reporter assessed the causal relationship between events and SILAPO as not related.
DE-STADA-058364 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-008-B031	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-03-19 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Retinal artery occlusion Onset: 2012-11-23 Outcome: recovered with sequel	Retinal artery occlusion / epoetin zeta: unlikely related	Retinal artery occlusion / epoetin zeta: not assessable	Retinal artery occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Mar-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenous weekly since 2012-Mar-19 for renal anemia. On 2012-Nov-23 the patient developed central retinal artery occlusion of left eye and was hospitalised. Therapy with pentoxifylline and rheologic optimization were conducted. The event resolved with sequelae and the patient was discharged on 2012-Nov-29. The reporter assessed the causal relationship to SILAPO as unlikely related.
DE-STADA-058365 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B031	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2012-03-19 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2013-01-30 Outcome: recovered	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Mar-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 18000 IU intravenous weekly since 2012-Mar-19 for renal anemia. On 2013-Jan-30 the patient developed ischemic stroke and was hospitalised. Therapy with coagulation inhibitor was conducted. The event resolved and the patient was discharged on 2013-Feb-15. The reporter assessed the causal relationship to SILAPO as unlikely related. Cross ref.: DE-STADA-058364 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-067531 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B031	80 to 89	Female	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Haemoglobin decreased Onset: 2013-09-05 Outcome: recovered Fall Onset: 2013-09-05 Outcome: recovered Syncope Onset: 2013-09-05 Outcome: recovered Traumatic haematoma Onset: 2013-09-05 Outcome: recovered	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Oct-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 15000 IU intravenous weekly since 2012-Mar-19 for renal anemia. On 2013-Sep-05 the patient developed hemoglobin decrease after fall due to syncope and hematoma on right thigh. The patient was hospitalised. The events resolved on 2013-Sep-09 and the patient was discharged. The reporter assessed the causal relationship to SILAPO as not related. Cross ref.: DE-STADA-058364, DE-STADA-058365 (same patient) Follow-up information #1 was received on 2013-Dec-30: On 2013-Sep-05 the patient developed hematoma of right thigh after a fall. The patient was hospitalised and the hematoma was sucked off. The event resolved on 2013-Oct-11. The reporter assessed the causal relationship to SILAPO as not related.
DE-STADA-080005 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B031	90 to 99	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-03-19 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Haemoglobin decreased Onset: 2014-04-17 Outcome: recovered Conjunctivitis Onset: 2014-04-17 Outcome: recovered	Conjunctivitis / epoetin zeta: not related Haemoglobin decreased / epoetin zeta: not related	Conjunctivitis / epoetin zeta: not related Haemoglobin decreased / epoetin zeta: unlikely related	Conjunctivitis / epoetin zeta: not applicable Haemoglobin decreased / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jun-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenous weekly since 2012-Mar-19 for renal anemia. On 2014-Apr-17 a hemoglobin decrease of unknown origin was detected and the patient was hospitalised. While hospitalised the patient developed conjunctivitis. The events were treated with erythrocytes concentrates and dexagent eye drops. The events resolved on 2014-Apr-23 and the patient was discharged. The reporter assessed the causal relationship to SILAPO as not related. Cross ref.: DE-STADA-058364, DE-STADA-058365, DE-STADA-067531 (same patient) Follow-up information #1 was received on 2014-Jul-04: The patient's hemoglobin level was 9.6 g/dl on 2014-Apr-15 7.6 g/dl on 2014-Apr-17 10.6 g/dl on 2014-Apr-24 13 g/dl in July 2014 and is stable at the time of report.
DE-STADA-126062 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-008-B035	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-01-07 End: 2016-09-15 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2016-06-26 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Cardiorenal syndrome Hypertensive nephropathy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-17 and on 2016-Oct-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously, 12000 IU weekly since 2015-Jan-07 for renal anemia. On 2016-Jun-26 the patient developed peripheral arterial occlusive disease with necrosis of right forefoot and was hospitalised. The patient underwent amputation of forefoot and was discharged on 2016-Sep-12. On 2016-Sep-14 the patient developed septic shock and died on 2016-Sep-15 (not related to SILAPO). The reporter assessed the causal relationship between peripheral arterial occlusive disease and SILAPO as not related. Medical history included hypertensive nephropathy and cardiorenal syndrome.
DE-STADA-089679 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-008-B037	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-08-16 End: 2014-11-10 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Pulmonary embolism Onset: 2014-11-11 Outcome: fatal	Pulmonary embolism / epoetin zeta: unlikely related	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenously weekly since 2012-Aug-16 for renal anemia. On 2014-Nov-11 the patient developed lung embolism and was hospitalised. Reanimitation was conducted but the patient died. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-173722 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-008-B038	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-02-25 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-10-15 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Dec-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Feb-25 for renal anemia. The current SILAPO dose was 3000 IU weekly (batch number not provided). On 2017-Oct-15 the patient developed myocardial infarction and was hospitalised. The patient died on 2017-Nov-13 due to cardiac failure. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included triple vessel disease.
DE-STADA-052335 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B043	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-01 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Device related infection Onset: 2012-09-24 Outcome: recovered	Device related infection / epoetin zeta: unlikely related	Device related infection / epoetin zeta: not related	Device related infection / epoetin zeta: not listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenous, 8000 IU weekly since 2011-Feb-01 for renal anemia. On 2012-Sep-24 she developed a dialysis catheter infection and was hospitalised. The catheter was replaced by a new one and the event resolved on 2012-Sep-27. The patient was discharged the same day. Medical history included hypertension since July 2009. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-064565 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B043	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-01 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt stenosis Onset: 2013-05-16 Outcome: recovered	Shunt stenosis / epoetin zeta: not related	Shunt stenosis / epoetin zeta: not assessable	Shunt stenosis / epoetin zeta: listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Aug-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously, 18000 IU weekly since 2011-Feb-01 for renal anemia. On 2013-May-16 the patient developed shunt vein stenosis (after multiple shunt revisions) and was hospitalised. The arteriovenous fistula was removed proximal. The event resolved on 2013-May-18 and the patient was discharged. Medical history included hypertension since July 2009. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-052335 (same patient).
DE-STADA-070614 v1.0	Yes Patient died Life threatening	DE-008-B049	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-04-25 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Death Onset: 2013-10-27 Outcome: fatal Cardiac failure Onset: 2013-10-27 Outcome: fatal	Cardiac failure / epoetin zeta: not assessable Death / epoetin zeta: not assessable	Cardiac failure / epoetin zeta: not assessable Death / epoetin zeta: not assessable	Cardiac failure / epoetin zeta: not listed Death / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU intravenously weekly since 2012-Apr-25 for renal anemia. On 2013-Oct-27 the patient was found dead at home. A decompensated cardiac insufficiency was suspected. The reporter assessed the causal relationship between the event and SILAPO as not assessable.
DE-STADA-053823 v1.0	Yes Patient died	DE-008-B059	50 to 59	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-07-04 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-11-14 Outcome: fatal	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: listed	Hypertension Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Nov-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 9000 IU weekly since 2012-Jul-04 for renal anemia. On 2012-Nov-14 the patient developed lung embolism and died the same day. Medical history included obesity and hypertension since September 2007. The reporter assessed the causal relationship between event and SILAPO as possible related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-119688 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B071	70 to 79	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2014-07-03 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2015-12-08 Outcome: recovered	Transient ischaemic attack / epoetin zeta: unlikely related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jun-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Jul-03 for renal anemia. The current dose was 1000 IU weekly. On 2015-Dec-08 the patient was hospitalised with transient ischemic attack with specific symptoms. Therapy for the event was adjusting the Marcumar (INN: phenprocoumon) dose and reduction of diuretics. The event resolved 2015-Dec-08 and the patient was discharged on 2015-Dec-11. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-089745 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B072	50 to 59	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-12-06 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt occlusion Onset: 2014-07-09 Outcome: recovered	Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly intravenously since 2013-Dec-06 for renal anemia. On 2014-Jul-09 the patient developed shunt dysfunction of upper arm shunt left and skin lesion at PTFE graft and was hospitalised. Therapy for the event was shunt revision. The event resolved on 2014-Jul-12 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-089675 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B073	50 to 59	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Transient ischaemic attack Onset: 2014-07-29 Outcome: recovered	Transient ischaemic attack / epoetin zeta: unlikely related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) IV 1000 IU weekly since 2013-Oct-23 for renal anemia. On 2014-Jul-29 the patient developed a transient ischemic attack and was hospitalised. The event was treated with acetylsalicylic acid and clopidogrel. The event resolved on 2014-Aug-01 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-104251 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B073	50 to 59	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous bolus	N/A	Transient ischaemic attack Onset: 2015-08-21 Outcome: recovered	Transient ischaemic attack / epoetin zeta: unlikely related	Transient ischaemic attack / epoetin zeta: unlikely related	Transient ischaemic attack / epoetin zeta: listed	Immune thrombocytopenic purpura Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Sep-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly, intravenously since 2013-Oct-23 for renal anemia. On 2015-Aug-14 the patient developed a transient ischemic attack and was hospitalised. The event was treated with platelet inhibition and anticoagulation therapy. The event resolved on 2015-Aug-21 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included idiopathic thrombocytopenic purpura started in 2005. Cross ref.: DE-STADA-089675 (same patient, same event).
DE-STADA-109087 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B081	90 to 99	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-22 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous bolus	N/A	Transient ischaemic attack Onset: 2015-09-05 Outcome: recovered with sequel	Transient ischaemic attack / epoetin zeta: not related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Dec-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) intravenously since 2013-Oct-22 for renal anemia. The current dose was 6000 IU weekly. On 2015-Sep-05 the patient developed a transient ischemic attack with specific symptoms and was hospitalised. The event resolved with sequelae on 2015-Sep-15 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-104248 v3.0	Yes Other medical important condition	DE-008-B082	80 to 89	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-22 End: 2015-04-28 Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Intravenous bolus	N/A	Drug ineffective Onset: 2015-04-28 Outcome: unknown Haemoglobin decreased Onset: 2015-04 Outcome: recovered	Drug ineffective / epoetin zeta: probable related Haemoglobin decreased / epoetin zeta: possible related	Drug ineffective / epoetin zeta: possible related Haemoglobin decreased / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed Haemoglobin decreased / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Sep-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 15000 IU weekly intravenously since 2013-Oct-22 for renal anemia. Despite high dose therapy with SILAPO a lack of drug effect was noted. The therapy with SILAPO was withdrawn on 2015-Apr-28. The patient changed to Neorecormon (INN: epoetin beta). The reporter assessed the causal relationship between event and SILAPO as probably related. Follow-up information #1 was received on 2015-Nov-09: The haemoglobin value at start of SILAPO was 10.4 g/dl. The haemoglobin values decreased to 8.4 g/dl in April 2015. After discontinuation of SILAPO and change to Neorecormon 3 x 5000 IE (INN: epoetin beta) the haemoglobin values increased (10.8 g/dl in September 2015). Follow-up information #2 was received on 2015-Dec-02: Neorecormon was administered 3 x 5000 IE weekly. The batch numbers of SILAPO (administered in the last 5 months) was 4X075X4 and 4V059V4.
DE-STADA-089678 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B087	50 to 59	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt occlusion Onset: 2014-11-25 Outcome: recovered	Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly intravenously since 2013-Oct-23 for renal anemia. On 2014-Nov-25 the patient developed stenosis induced shunt occlusion and was hospitalised. Therapy for the event was shunt revision and substitution of interposition graft. The event resolved on 2014-Nov-29 and the patient was discharged. The therapy with SILAPO was interrupted on 2014-Nov-21. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-093921 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-008-B087	50 to 59	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2014-12-28 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Mar-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly intravenously since 2013-Oct-23 for renal anemia. On 2014-Dec-28 the patient developed ischaemic stroke and was hospitalised. The patient was discharged on 2015-Jan-20 and recovered with sequelae. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included adipositas. Cross ref.: DE-STADA-089678 (same patient).
DE-STADA-109067 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-008-B087	60 to 69	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2015-10-23 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Dec-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) intravenously since 2013-Oct-23 for renal anemia. The current dose was 12000 IU weekly. On 2015-Oct-23 the patient suffered from deterioration of pre-existing hemiparesis and was hospitalised. An ischaemic stroke was diagnosed. The patient underwent lysis therapy. The event resolved and the patient was discharged on 2015-Nov-03 with disability. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-089678, DE-STADA-093921 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-126064 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-008-B087	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-10-23 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Cerebrovascular accident Onset: 2016-08-02 Outcome: recovered	Cerebrovascular accident / epoetin zeta: unlikely related	Cerebrovascular accident / epoetin zeta: unlikely related	Cerebrovascular accident / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2013-Oct-23 for renal anemia. The current dose was 9000 IU weekly. On 2016-Aug-02 the patient developed a transient ischemic attack and corresponding syndromes (arteria cerebri media left symptom with hemiparesis of right site and symptomatic epilepsy) and was hospitalised. The patient underwent therapeutic anticoagulation (no change of pretreatment). The event resolved and the patient was discharged on 2016-Aug-04. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-089678, DE-STADA-093921, DE-STADA-109067 (same patient)
DE-STADA-043920 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-009-B003	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-29 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebrovascular accident Onset: 2011-06-30 Outcome: recovered Dysarthria Onset: 2011-06-30 Outcome: recovered	Cerebrovascular accident / epoetin zeta: not related Dysarthria / epoetin zeta: not related	Cerebrovascular accident / epoetin zeta: not assessable Dysarthria / epoetin zeta: not assessable	Cerebrovascular accident / epoetin zeta: listed Dysarthria / epoetin zeta: listed	Dysuria Hypertensive heart disease Nephrogenic anaemia Parkinson's disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-Jun-29 for renal anemia. On 2011-Jun-30 the patient developed slurred speech and a stroke was suspected. The patient was hospitalised and neurological and antihypertensive treatment was performed. The event resolved on 2011-Jul-04. Medical history included Parkinson's disease, hypertensive cardiac disease and voiding disorder. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-049947 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-009-B018	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-05-18 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-01-12 Outcome: recovered Pneumonia Onset: 2012-01-12 Outcome: recovered	Pneumonia / epoetin zeta: unlikely related Pulmonary embolism / epoetin zeta: unlikely related	Pneumonia / epoetin zeta: not assessable Pulmonary embolism / epoetin zeta: not assessable	Pneumonia / epoetin zeta: not listed Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 8000 IU weekly since 2011-May-18 for renal anemia. On 2012-Jan-12 the patient developed right sided pulmonary embolism with infarction pneumonia and was hospitalised. The patient received oral anticoagulance therapy with Falithrom and the event resolved on 2012-Jan-27. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-061575 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-010-B001	unknown	Male	SILAPO InjektionsÃ¶sung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: unknown	N/A	Ischaemic stroke Onset: 2012-11-20 Outcome: recovered	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: possible related	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-May-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia An elderly male patient started receiving SILAPO InjektionsÃ¶sung in Fertigspritze (INN: epoetin zeta) subcutanously 6000 I.U. weekly on 2011-Jan-31 for renal anaemia. On 2012-Nov-20 he suffered from ischaemic stroke. The patient was hospitalised due to the event on 2012-Nov-20 and discharged on 2012-Dec-06. The event was treated with acetylsalicylic acid therapy, stoke specific physiotherapy and logopedic therapy. The outcome was reported to be recovered on 2012-Nov-21. The epoetin zeta therapy was still ongoing. The reporter assessed the causal relationship between suspected drug and event as unlikely related.
DE-STADA-074399 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-010-B003	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Mesenteric vein thrombosis Onset: 2013-12-17 Outcome: fatal Gastrointestinal necrosis Onset: 2013-12-16 Outcome: fatal Intestinal infarction Onset: 2013-12-16 Outcome: fatal	Gastrointestinal necrosis / epoetin zeta: unlikely related Intestinal infarction / epoetin zeta: unlikely related Mesenteric vein thrombosis / epoetin zeta: unlikely related	Gastrointestinal necrosis / epoetin zeta: not assessable Intestinal infarction / epoetin zeta: not assessable Mesenteric vein thrombosis / epoetin zeta: not assessable	Gastrointestinal necrosis / epoetin zeta: not listed Intestinal infarction / epoetin zeta: not listed Mesenteric vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Mar-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) for renal anemia since 2011-Jan-31. On 2013-Dec-08 the patient was hospitalised for laparotomy. Examination revealed gastric reflux of small intestine contents with peritonism. A CT scan showed mesenteric infarction with small intestinal necrosis and peritonitis. Postoperatively the patient developed septic shock with therapy refractory lactic acidosis on 2013-Dec-16. The patient died on 2013-Dec-17 due to septic shock, community-acquired pneumonia and mesenteric thrombosis. The reporter assessed the causal relationship between events and SILAPO as unlikely related. Follow-up information #1 was received on 2014-Dec-12: SILAPO was administered 4000 IU weekly subcutaneously.
DE-STADA-036445 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-010-B005	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-01 End: 2011-05-03 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt thrombosis Onset: 2011-05-03 Outcome: recovered	Shunt thrombosis / epoetin zeta: unlikely related	Shunt thrombosis / epoetin zeta: not assessable	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Jun-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 9N116DO, SC 3000 IU weekly since 2011-Feb-01 for renal anemia. On 2011-May-03 the patient was hospitalised due to a thrombosed shunt aneurysm of the left arm. An excision of the shunt aneurysm was performed and the event resolved. The patient was discharged on 2011-May-09. The reporter assessed the causal relationship between event and SILAPO as unlikely.
DE-STADA-038583 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-010-B005	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-01 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-08-23 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Aug-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1F218H1, SC 6000 IU weekly since 2011-Feb-01 for renal anemia. The patient was hospitalised since 2011-Aug-16 for a shunt infection at left forearm. On 2011-Aug-24 the patient developed myocardial infarction and was transferred to the intensive case unit. The patient died on 2011-Aug-26. The reporter assessed the causal relationship between event and SILAPO as not related. Cross reference: DE-STADA-036445 (same patient). Follow-up information 1 was received on 2012-Jul-17: The reaction onset date was corrected to 2011-Aug-23. No further new information was provided.
DE-STADA-035112 v2.0	Yes Patient died	DE-010-B013	90 to 99	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 1500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	Einsalpha 0.25 INN: alfacalcidol Indication: Product used for unknown indication Ferrlecit INN: iron Indication: Product used for unknown indication	Ischaemic stroke Onset: 2011-04-01 Outcome: fatal	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Bladder cancer Bladder catheterisation Nephrogenic anaemia Presbyacusis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-May-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 9N116D0, SC 1500 IU weekly since 2011-Jan-31 for renal anemia. On 2011-Apr-01 the patient was hospitalised due to ischemic stroke. On 2011-Apr-12 the patient died due to stroke. An autopsy was not performed. Concomitant medication was Einsalpha 0.25 (INN: alfacalcidol) 0.25Âµg 2 times weekly since 2010-Oct-25 and Ferrlecit (INN: iron) 62.5 mg every 3 weeks from 2009-Sep-16 to 2011-Mar-16. The patient's medical history included urinary bladder carcinoma in September 2009, bladder catheter and presbyacusis. The reporter assessed the causal relationship between event and SILAPO as unlikely. Follow-up #1 was received on 2011-May-17 from the physician. The patient died due to widespread infarction of A. cerebri media on the right. The patient suffered from clouding of consciousness and facial paresis during dialysis with stable circulation. Diagnosis of ischemic stroke was confirmed by cranial CT.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-041331 v3.0	Yes Patient died	DE-013-B004	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-27 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-09-16 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Arrhythmia Arterial bypass operation Atrial fibrillation Cardiac pacemaker insertion Carotid artery stenosis Cholelithiasis Chronic obstructive pulmonary disease Convulsion Coronary artery disease Myocardial infarction Myocardial ischaemia Peripheral arterial occlusive disease Renal failure chronic Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Nov-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 6000 IU weekly from 2011-May-27 for renal anemia. On 2011-Nov-07 the patient died due to myocardial infarction. Patient's medical history included coronary heart disease. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up#1 information was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-13. The patient developed myocardial infarction on 2011-Sep-16 and not on 2011-Nov-07 as previously reported and died on 2011-Sep-17. Follow-up#2 information was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-15. Patient's medical history included chronic ischemic heart disease, condition after myocardial infarction and bypass surgeries, arrhythmia with atrial fibrillation, pacemaker insertion, peripheral occlusive disease, chronic renal insufficiency, diabetes mellitus type 2, seizures, COPD, carotis stenosis, cholecystolithiasis. The last measured lab values revealed normocytic anemia with Hb 7.1.
DE-STADA-044375 v1.0	No	DE-014-B001	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-03-25 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pruritus Onset: 2011-04 Outcome: recovered	Pruritus / epoetin zeta: possible related	Pruritus / epoetin zeta: possible related	Pruritus / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Mar-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 4000 IU weekly since 2011-Mar-25 for renal anemia. In April 2011 he developed pruritus which lasted until February 2012 before abated. SILAPO was paused on 2011-Apr-20 and now reintroduced. The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-052413 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-014-B007	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2011-07-25 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Coronary artery disease Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 4000 IU weekly since 2011-Jan-31 for renal anemia. On 2011-Jul-25 he developed thoracic pain and dyspnoea diagnosed as unstable angina pectoris. The patient was hospitalised. The event resolved and the patient was discharged on 2011-Aug-03. Patient's medical history included coronary heart disease since 1995 and obesity. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-068109 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-014-B007	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2013-06-27 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Hypertension Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenously weekly since 2011-Jan-31 for renal anemia. On 2013-Jun-27 the patient was hospitalised with thoracic pain and a myocardial infarction was diagnosed. A percutaneous transluminal angioplasty and coronary stent implant was performed. The event resolved and the patient was discharged on 2013-Jul-10. Patient's medical history included coronary heart disease since 1995, hypertension since 1960 and obesity. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-052413, DE-STADA-068110 (same patient).
DE-STADA-068110 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-014-B007	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-01-31 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Arterial occlusive disease Onset: 2013-09-10 Outcome: recovered	Arterial occlusive disease / epoetin zeta: unlikely related	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: listed	Coronary artery disease Hypertension Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenously weekly since 2011-Jan-31 for renal anemia. On 2013-Sep-10 the patient developed acute arterial occlusion left lower leg and was hospitalised for embolectomy. The event resolved and the patient was discharged on 2013-Sep-16. Patient's medical history included coronary heart disease since 1995, hypertension since 1960 and obesity. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-052413, DE-STADA-068110 (same patient)
DE-STADA-067456 v2.0	No	DE-015-B003	70 to 79	Male	clonidine INN: clonidine Start: not stated End: not stated Dosage: not stated Dosage text: not stated RoA: unknown SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-10-21 End: 2013-10-14 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Dyskinesia Onset: 2013-09-06 Outcome: recovered	Dyskinesia / clonidine: possible related Dyskinesia / epoetin zeta: unlikely related	Dyskinesia / clonidine: possible related Dyskinesia / epoetin zeta: possible related	Dyskinesia / clonidine: not listed Dyskinesia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Oct-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2J300J2, 6000 I.E. weekly subcutaneously since 2011-Oct-21 for renal anemia. Since 2013-Sep-06 the patient suffered from involuntary face tics. The treatment with SILAPO was paused and the concomitant medication clonidine was tapered. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up information #1 was received on 2013-Dec-03: The concomitant medication clonidine was discontinued and the therapy with SILAPO was restarted with 8000 IU weekly. The event resolved on 2013-Nov-11 and did not reoccur. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-057791 v3.0	No	DE-015-B008	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-24 End: 2012-12-30 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Eczema Onset: 2012-12-03 Outcome: recovered	Eczema / epoetin zeta: possible related	Eczema / epoetin zeta: possible related	Eczema / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Feb-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 3000 I.E. weekly subcutaneously since 2012-Feb-24 for renal anemia. On 2012-Dec-03 the patient developed severe itching eczema of hands, legs, knees and tighs which was not resolved at the time of report. The treatment with SILAPO was intercepted. The reporter assessed the causal relationship between event and SILAPO as possible related. Medical history inlcuded coronary threevessel disease since 1998. Follow-up information #1 was received on 2013-May-10: The patient discontinued the PASCO II study. The event was resolved meanwhile. Follow-up information #2 was received on 2013-Sep-05: The eczema resolved on 2013-May-08. SILAPO therapy was discontinued on 2012-Dec-30.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-042539 v4.0	Yes Other medical important condition	DE-017-B007	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-02-28 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Retinal vein thrombosis Onset: 2011-03 Outcome: recovered	Retinal vein thrombosis / epoetin zeta: not related	Retinal vein thrombosis / epoetin zeta: not assessable	Retinal vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2011-Feb-28 for renal anemia. In March 2011 the patient developed a central vein thrombosis of left eye. The reporter's causal relationship was not provided. No further information was provided. Follow-up #1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jun-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. The suspected drug was withdrawn due to the event. The reporter's assessment remained still unknown. Follow-up information #2 was received on 2015-Jul-13: The patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU weekly subcutaneously. SILAPO was withdrawn. The event resolved. The reporter assessed the causal relationship as unrelated to SILAPO. Follow-up information #3 was received on 2015-Jul-24: The event resolved in Mar 2011. The SILAPO administration was not changed. The event did not reoccur.
DE-STADA-041361 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-019-B001	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-30 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2011-08-07 Outcome: not recovered	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	N/A	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 2000 IU weekly since 2011-Jun-30 for renal anemia. On 2011-Aug-07 the patient was hospitalised due to ischemic stroke after discontinuation of phenprocoumon due increased bleeding tendency. Phenprocoumon was replaced with fondaparinux. The patient was discharged on 2011-Aug-23 with sequelae. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-056363 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-019-B005	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-04-06 End: 2012-12-16 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2012-12-19 Outcome: unknown	Ischaemic stroke / epoetin zeta: possible related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jan-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-Apr-06 for renal anemia. In December 2012 the patient was hospitalised due to ischemic stroke. The outcome of the event was unknown. The reporter assessed the causal relationship between event and SILAPO as possibly related. Follow-up #1 was received was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-26. The date of event onset was 2012-Dec-19 and the event was life-threatening. The last administration of SILAPO prior to the event was 2012-Dec-16. Treatment with SILAPO was discontinued and the patient finished study preliminary.
DE-STADA-041360 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-019-B008	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-03-14 End: 2011-05-03 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2011-04-01 Outcome: recovered	Deep vein thrombosis / epoetin zeta: not related	Deep vein thrombosis / epoetin zeta: not assessable	Deep vein thrombosis / epoetin zeta: listed	Benign prostatic hyperplasia Nephrogenic anaemia Prostatic operation	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-Mar-14 for renal anemia. In April 2011 the patient was hospitalised due to deep vein thrombosis of the lower limbs possibly related to a prostatic surgery in March 2011. The patient was treated with anticoagulation therapy and the event resolved on 2011-Apr-30. The patient's medical history included prostatic hypertrophy from October 2010 to February 2011. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2014-Feb-17: The date of event was specified to 2011-Apr-01.
DE-STADA-052470 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-019-B010	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-05-24 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-07-15 Outcome: recovered	Pulmonary embolism / epoetin zeta: not related	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Chronic obstructive pulmonary disease Hypertensive heart disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-May-25 for renal anemia. On 2012-Jul-15 the patient developed pulmonary embolism and was hospitalised. The event resolved on 2012-Jul-26 and the patient was discharged. Medical history included chronic obstructive lung disease and hypertensive heart disease. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-043052 v1.0	Yes Patient died	DE-019-B021	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-08-29 End: 2011-12-26 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-12-26 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 8000 IU weekly since 2011-Aug-29 for renal anemia. On 2011-Dec-26 the patient died due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-051493 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-019-B022	unknown	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-04-20 End: 2012-06-01 Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2012-07-12 Outcome: recovered	Deep vein thrombosis / epoetin zeta: not related	Deep vein thrombosis / epoetin zeta: not assessable	Deep vein thrombosis / epoetin zeta: listed	Laceration Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Sep-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia An adult male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) from 2012-Apr-20 till 2012-Jun-01. On 2012-Jun-04 he had an accident at work with a laceration on his left lower leg. He was hospitalised due to deep vein thrombosis in his left leg (thigh and lower leg). The event was treated with heparin and afterwards with Marcumar (INN: phenprocoumon). The outcome was reported to be recovered. The reporter assessed the causal relationship between suspected drug and event as not related. Follow-up #1 was created on 2012-Oct-04 after internal case review in order to fill in the land of occurence Germany in the structured field.
DE-STADA-073227 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-019-B035	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-10-17 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2013-12-15 Outcome: recovered	Transient ischaemic attack / epoetin zeta: not related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 2000 IU weekly since 2011-Oct-17 for renal anemia. On 2013-Dec-15 during a routine control the patient complained of weakness in left hand for 4 weeks. A sonography revealed transient ischemic attacks. A surgical measure was recommended. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2014-May-06: The event was life-threatening and required hospitalisation on 2014-Jan-14. The event resolved on 2014-Jan-15 and the patient was discharged on 2014-Jan-30.
DE-STADA-063918 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-019-B042	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-11-14 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Retinal vein thrombosis Onset: 2012-02-01 Outcome: recovered	Retinal vein thrombosis / epoetin zeta: unlikely related	Retinal vein thrombosis / epoetin zeta: not assessable	Retinal vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jul-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 I.E. weekly subcutaneously since 2011-Nov-14 for renal anemia. On 2012-Feb-01 the patient developed venous thrombosis of right eye and was hospitalised. The patient underwent conservative treatment and recovered. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2014-Mar-05: The event resolved on 2012-Apr-20.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-039013 v2.0	Yes Patient died	DE-021-B013	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-22 End: not stated Dosage: 1 x 16000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-09-01 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Myocardial infarction	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Sep-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1F224H1, SC 16000 IU weekly since 2011-Feb-22 for renal anemia. The patient was hospitalised on 2011-Aug-30 for a colonoscopy and developed myocardial infarction on 2011-Aug-31. The patient was transferred to the intensive case unit and died on 2011-Sep-02. Medical history included coronary heart disease with myocardial infarction in July 1990. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up #1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Sep-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. The patient was hospitalised on 2011-Aug-30 for the clarification of stool abnormalities and recurrent diarrhoea. On 2011-Sep-01 the patient developed acute myocardial infarction at pre-existing coronary heart disease. She was transferred to the intensive care unit and died on 2011-Sep-02. Lab value for hemoglobin was 11.9 g/dl on 2011-Aug-31, 11.6 g/dl on 2011-Sep-01 and 10.8 g/dl on 2011-Sep-02. Lab value for hematocrit was 0.38 on 2011-Aug-31, 0.37 on 2011-Sep-01 and 0.35 on 2011-Sep-02.
DE-STADA-046942 v1.0	Yes Patient died	DE-021-B014	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-02-21 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-05-05 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Aortic valve replacement Cardiac pacemaker insertion Coronary artery disease Diabetic nephropathy Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-May-08. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 4000 IU per week since 2011-Feb-21 for renal anemia. On 2012-May-05 the patient died due to myocardial infarction. Patient's medical history included renal insufficiency due to diabetic nephropathy, insulin-dependent diabetes mellitus type 2, coronary heart disease, aortic valve replacement and pacemaker insertion. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-045877 v1.0	Yes Life threatening	DE-022-B005	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-01-24 End: 2012-03-27 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arrhythmia Onset: 2012-03-21 Outcome: not recovered Dizziness Onset: 2012-03-21 Outcome: not recovered Somnolence Onset: 2012-03-21 Outcome: not recovered	Arrhythmia / epoetin zeta: probable related Dizziness / epoetin zeta: probable related Somnolence / epoetin zeta: probable related	Arrhythmia / epoetin zeta: possible related Dizziness / epoetin zeta: possible related Somnolence / epoetin zeta: possible related	Arrhythmia / epoetin zeta: not listed Dizziness / epoetin zeta: listed Somnolence / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Apr-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 2000 IU weekly since 2012-Jan-24 for renal anemia. On 2012-Mar-21 the patient developed dizziness, drowsiness and arrhythmia. According to the reporter the events were life-threatening. The patient was not hospitalised. SILAPO was withdrawn on 2012-Mar-27. At the time of report the events were not resolved. Patient's medical history included obesity. The reporter assessed the causal relationship between events and SILAPO as probably related.
DE-STADA-147090 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-022-B006	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-09-23 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2017-05-22 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Sep-23 for renal anemia. The current SILAPO dose was 4000IU weekly. On 2017-May-22 the patient was hospitalised due to myocardial infarction. A bypass was inserted and the patient was discharged on 2017-Jun-01. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-181430 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-022-B011	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2014-02-28 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2017-04-10 Outcome: recovered	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2014-Feb-28 for renal anemia. The current dose was 18000 IU weekly. Batch number not provided. On 2017-Apr-10 the patient developed ischaemic stroke and was hospitalised. The event resolved on 2019-Apr-14 and the patient was discharged. The therapy with SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-041817 v5.0	Yes Other medical important condition	DE-023-B005	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-06 End: 2011-12-23 Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: not stated Outcome: recovered	Drug ineffective / epoetin zeta: probable related	Drug ineffective / epoetin zeta: not assessable	Drug ineffective / epoetin zeta: listed	N/A	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 8000 IU weekly from 2011-Jun-06 for renal anemia. On 2011-Dec-23 the treatment with SILAPO was discontinued due to lack of drug effect and the patient changed to another drug ARANESP (INN: darbepoetin alfa). No further information was provided. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-03. Despite increase in SILAPO dose up to 24000 IU weekly the hemoglobin value did not improve. Therefore SILAPO was discontinued and the patient changed to another erythropoetin stimulating agent and the patient recovered. Follow-up#2 was received from a center nurse on 2012-Jan-23. Haemoglobin values were provided as 5.9 on 2011-Nov-02, 6 on 2011-Nov-16 and 5.9 on 2011-Nov-23 during Silapo therapy. After the switch to epoetin (unknown MAH) one haemoglobin test was performed and resulted in 7.3. Further reasons for decreased haemoglobin level as bleeding, increased Fe levels were excluded. Follow-up#3 report was generated on 2012-Feb-16 after internal case review in order to add the Sponsor's study number in the structured field. Follow-up#4 was received on 2012-Aug-23: The reporter assessed the causal relationship as probably related.
DE-STADA-043693 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-023-B010	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-06 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Angina unstable Onset: 2012-01-13 Outcome: not recovered	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) IV 8000 IU weekly since 2011-Jun-06 for renal anemia. On 2012-Feb-03 the patient developed an unstable angina pectoris and was hospitalised. At the time of report the outcome of the event was unknown. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jun-26. The date of event and hospitalisation was corrected to 2012-Jan-13. The patient was discharged on 2012-Jan-17 and received continuative treatment. The event was not resolved at the time of report. The administered SILAPO batch was 1F224H1/03-2013.
DE-STADA-043694 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-023-B013	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-06 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Tachycardia Onset: 2012-01-17 Outcome: unknown	Tachycardia / epoetin zeta: not assessable	Tachycardia / epoetin zeta: unlikely related	Tachycardia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Feb-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) IV 4000 IU weekly since 2011-Jun-06 for renal anemia. On 2012-Jan-17 the patient developed tachycardia under dialysis and was hospitalised. The patient was discharged on 2012-Jan-24. At the time of report the outcome of the event was unknown. The reporter assessed the causal relationship between event and SILAPO as not assessable.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-048772 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-023-B013	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-06-06 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ventricular arrhythmia Onset: 2012-02-27 Outcome: unknown Atrial fibrillation Onset: 2012-02-27 Outcome: unknown	Atrial fibrillation / epoetin zeta: not assessable Ventricular arrhythmia / epoetin zeta: not assessable	Atrial fibrillation / epoetin zeta: not related Ventricular arrhythmia / epoetin zeta: not related	Atrial fibrillation / epoetin zeta: not listed Ventricular arrhythmia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jun-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), batch: 1F221H1/03-2013, IV 4000 IU weekly since 2011-Jun-06 for renal anemia. On 2012-Feb-27 the patient developed absolute ventricular arrhythmia associated with atrial fibrillation and was hospitalised. The patient underwent transesophageal echocardiography and was discharged on 2012-Mar-05. At the time of report the outcome of the event was unknown. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-049663 v2.0	Yes Other medical important condition	DE-025-B007	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-05-27 End: 2012-02-23 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2012-01-04 Outcome: recovered Shunt occlusion Onset: 2012-07-06 Outcome: not recovered	Shunt occlusion / epoetin zeta: unlikely related Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2011-May-27 for renal anemia. On 2012-Jan-04 the patient developed shunt occlusion of right forearm which resolved the same day. On 2012-Jul-06 she again developed shunt occlusion of the right forearm which was not resolved at the time of report. The reporter did not assess the causal relationship between event and SILAPO. Follow-up information #1 was received on 2012-Aug-06: A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2011-May-27 for renal anemia. On 2012-Jan-04 the patient developed shunt occlusion of right forearm which resolved the same day. Therapy with SILAPO was discontinued on 2012-Feb-23. The reporter assessed the causal relationship between event and SILAPO as not related. On 2012-Jul-06 the patient again developed shunt occlusion of the right forearm which was not resolved at the time of report. Medical history inlcuded obesity. The reporter assessed the causal relationship between event and SILAPO as unlikely.
DE-STADA-052282 v1.0	No	DE-026-B011	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-05-10 End: 2012-09-28 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Dermatitis allergic Onset: not stated Outcome: unknown	Dermatitis allergic / epoetin zeta: possible related	Dermatitis allergic / epoetin zeta: possible related	Dermatitis allergic / epoetin zeta: listed	N/A	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-May-10 for renal anemia. On 2012-Sep-28 the patient discontinued the study because of allergic exanthema on arms and legs after each SILAPO administration. The patient changed to ERYPO 2000.
DE-STADA-082196 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-026-B012	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-08-01 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2014-06-17 Outcome: fatal	Myocardial infarction / epoetin zeta: possible related	Myocardial infarction / epoetin zeta: possible related	Myocardial infarction / epoetin zeta: listed	Aortic valve stenosis Cardiac pacemaker insertion Coronary artery disease Hyperlipidaemia Hypertension Nephrogenic anaemia Obesity Renal failure chronic Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Aug-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 1000 IU weekly subcutaneously since 2011-Aug-01 for renal anemia. On 2014-Jun-17 the patient developed myocardial infarction. The patient was hospitalised on 2014-Jun-27. Despite several percutaneous coronary interventions the patient died on 2014-Jul-27 due to cardiogenic shock. Patient's medical history included aortic valve stenosis, threevessel disease, insertion of pacemaker, chronic renal insufficiency, diabetes mellitus type 2, hypertension, adipositas and hyperlipoproteinemia. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up information #1 was received on 2014-Dec-01: At start of treatment with SILPAO the patient received 700 IU weekly. Prior to the event the patient received 1000 IU every 10 days.
DE-STADA-085642 v2.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-026-B019	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-12-12 End: 2014-05-10 Dosage: 1 x 700 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2014-07-23 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Atrial fibrillation Cardiac failure Cerebellar haematoma Diabetic retinopathy Hypercholesterolaemia Hyperparathyroidism Hypertensive heart disease Hyperuricaemia Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Obesity Pleural effusion Polyneuropathy Pulmonary congestion Renal failure chronic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 3000 IU weekly subcutaneously since 2011-Dec-12 for renal anemia. On 2014-Jul-23 the patient developed ischemic stroke after anticoagulant therapy (phenprocoumon) was paused due to bleeding. The patient was hospitalised and anticoagulant therapy with apixaban was started. The patient was discharged on 2014-Aug-02 with sequelae. SILAPO treatment was interrupted on 2014-Jul-23. The last administration of SILAPO before event onset was 2014-Jul-17. Patient's medical history included left heart decompensation with pulmonary congestion and pleural effusion, hypertensive heart disease, sub- and epidural hematoma in cerebellum under phenprocoumon and acetylsalicylic acid therapy in May 2014, chronic renal insufficiency, renale anemia, obesity, chronic atrial fibrillation, hyperparathyroidism, hyperuricemia, diabetic retinopathy, polyneuropathy, diabetes mellitus type 2 and hypercholesterolemia. The reporter assessed the causal relationship between event and SILAPO as possibly related. Follow-up information #1 was received on 2014-Oct-16: SILAPO therapy was discontinued on 2014-May-14. The last administration of SILAPO with 700 IU weekly subcutaneously before event was 2014-May-10. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-085723 (same patient)
DE-STADA-085723 v2.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-026-B019	70 to 79	Female	clopidogrel INN: clopidogrel Start: 2013-08-12 End: 2014-05-14 Dosage: 1 x 75 mg per every 1 Day Dosage text: not stated RoA: unknown Marcumar INN: phenprocoumon Start: 2009-05-29 End: 2014-05-14 Dosage: not stated Dosage text: not stated RoA: unknown SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-12-12 End: 2014-05-10 Dosage: 1 x 700 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebellar haematoma Onset: 2014-05-15 Outcome: recovered with sequel	Cerebellar haematoma / clopidogrel: possible related Cerebellar haematoma / epoetin zeta: unlikely related Cerebellar haematoma / phenprocoumon: possible related	Cerebellar haematoma / clopidogrel: possible related Cerebellar haematoma / epoetin zeta: not assessable Cerebellar haematoma / phenprocoumon: possible related	Cerebellar haematoma / clopidogrel: listed Cerebellar haematoma / epoetin zeta: listed Cerebellar haematoma / phenprocoumon: not applicable	Atrial fibrillation Cardiac failure Drug intolerance Gastrointestinal haemorrhage Hypercholesterolaemia Hyperparathyroidism Hypertension Hyperthyroidism Hypokalaemia Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Nephropathy Obesity Peripheral arterial occlusive disease Polyneuropathy Postrenal failure Restless legs syndrome Retinopathy Urinary tract infection	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 700 IU weekly subcutaneously since 2011-Dec-12 for renal anemia. The patient was hospitalised due to derailed diabetes mellitus. In hospital decreased Quick's value under Marcumar (INN: phenprocoumon) was detected (8%). On 2014-May-14 a cranial computer tomography showed subdural hematoma at cerebellum (brain hemorrhage), brain ventricle compression. The event resolved. There was no change in SILAPO treatment. Patient's medical history included obesity and chronic atrial fibrillation. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-085642 (same patient) Follow-up information #1 was received on 2014-Oct-16 and on 2014-Oct-20: The event resolved on 2014-May-28 and the patient was discharged. The patient recovered with sequelae. SILAPO therapy was discontinued on 2014-May-14. The last administration of SILAPO before event was 2014-May-10. The reporter assessed the causal relationship between event and SILAPO as unlikely related. The brain hemorrhage was related to increased Quick level and clopidogrel intake. The co-medication Marcumar (INN: phenprocoumon) and clopidogrel were discontinued on 2014-May-14. Patient' medical history included hypokalemia, urinary tract infection, hypertension, heart insufficiency, arrhythmia absoluta, peripheral arterial occlusive disease, hypercholesterolemia, insulin-dependent diabetes mellitus type 2, polyneuropathy, restless leg syndrome, nephropathy, renal anemia, hyperparathyroidism, retinopathy, condition after renal failure, condition after gastrointestinal bleeding, hyperthyroidism and intolerance to metamizole.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-045603 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-026-B023	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-06 End: 2011-10-03 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-10-09 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Diabetes mellitus Diabetic nephropathy Hyperparathyroidism Hypertension Nephrogenic anaemia Renal tubular disorder	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Mar-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta), SC 2000 IU weekly since 2011-May-06 for renal anemia. On 2011-Oct-09 the patient developed myocardial infarction and was hospitalised. The patient was treated with acetylsalicylic acid, clopidogrel and heparin and recovered the same day. He was discharged on 2011-Oct-20. Patient's medical history included diabetic and tubulointerstitial nephropathy, diabetes mellitus, hypertension and hyperparathyroidism. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up #1 report was received from a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. The Silapo therapy was stopped on 2011-Oct-03.
DE-STADA-068910 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-026-B025	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-07-22 End: 2013-04-19 Dosage: not stated Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2013-05-28 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: listed	Hyperkalaemia Hypertension Hypothyroidism Nephrogenic anaemia Nephropathy Peripheral arterial occlusive disease Renal failure chronic Renal tubular acidosis Systemic lupus erythematosus Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) intravenously since 2011-Jul-22 for renal anemia. On 2013-May-28 a peripheral artery occlusive disease with lower leg gangrene was diagnosed which required amputation of left leg. The gangrene was due to longtime tobacco abuse and lupus erythematodes. At the time of event SILAPO was already paused since 2013-Apr-19. The patient recovered with sequelae. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Medical history included chronic renal insufficiency, interstitial nephropathy, hypertension, renal acidosis, hyperkaliemia, peripheral arterial disease, systemic lupus erythematodes and tobacco abuse.
DE-STADA-055653 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-026-B027	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-07-29 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-08-22 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Hyperlipidaemia Hypertension Metabolic acidosis Multiple myeloma Nephrogenic anaemia Osteolysis Renal failure Secondary hypothyroidism Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jan-07 and on 2013-Jan-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) 9000 I.E. weekly subcutaneously since 2011-Jul-29 for renal anemia. On 2012-Aug-22 the patient was hospitalised with non-ST elevating myocardial infarction. No intervention (coronary) was conducted at known thrombopenia (plasmocytoma). The patient was treated conservatively and the plasmocytoma was treated with cyclophosphamide and prednisolone. The event resolved on 2012-Sep-15 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history inlcuded renal insufficiency, hypertension, diabetes mellitus type 2, multiple myeloma, hyperlipidemia, secondary hypothyroidism, metabolic acidosis, osteolysis.
DE-STADA-069140 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-026-B034	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-07-28 End: 2013-05-19 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-05-19 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Aortic valve stenosis Hyperparathyroidism Hypertension Nephrogenic anaemia Nephrolithiasis Nephropathy Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2011-Jul-28 for renal anemia. On 2013-May-19 a myocardial infarction was suspected within a sepsis with increased troponin and ECG changes. The patient was hospitalised, a coronary angiography was not performed. The patient underwent bed rest and monitoring. She was discharged on 2013-May-31. On 2013-Jun-27 the patient died due to sepsis and pneumonia. Patient's medical history included aortic valve stenosis, renal insufficiency, vascular nephropathy, renal hyperparathyroidism, nephrolithiasis and hypertension. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2013-Nov-29: The dose of SILAPO was 8000 IU weekly.
DE-STADA-049665 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-027-B012	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-23 End: not stated Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-07-05 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Hepatitis B Hyperparathyroidism Monoclonal gammopathy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-16 and on 2012-Jul-25 respectively. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta), SC 5000 IU weekly since 2011-May-23 for renal anemia. The patient was hospitalised due to abdominal pain syndrome for an angiography. On 2012-Jul-05 during angiography the patient died due to myocardial infarction. Patient's medical history included hepatitis B, monoclonal gammopathy and secondary hyperparathyroidism. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-053022 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-027-B020	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-23 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2012-08-06 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: listed	Aortic valve stenosis Coronary artery disease Nephrogenic anaemia Sick sinus syndrome	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-24 and on 2012-Oct-25 respectively. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta), batch: 1N259C2, SC 10000 IU weekly since 2011-May-23 for renal anemia. On 2012-Aug-06 the patient developed unstable angina pectoris which was described as suspicion of angina pectrois with increased exertional dyspnoea adn dizziness. The patient was hospitalised on 2012-Oct-05. The event resolved on 2012-Oct-19 and the patient was discharged. Patient's medical history included aortic valve stenosis since June 2006, coronary heart disease since May 2011 and sick sinus syndrome with bradycardia since November 2007. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up#1 was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Nov-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia The reporter assessed the causal relationship between suspected drug and event as not related. Aortic valve replacement was planned.
DE-STADA-045188 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-027-B023	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-24 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-03-05 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Tachyarrhythmia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Mar-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta), batch: 1J24J31, SC 12000 IU weekly since 2011-May-24 for renal anemia. On 2012-Mar-05 the patient developed myocardial infarction and was hospitalised. The patient recovered on 2012-Mar-14. Patient's medical history included tachyarrhythmia absoluta since 2010-Jul. The reporter did not assess the causal relationship between event and SILAPO. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Mar-29. The reporter assessed the causal relationship between event and SILAPO as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-048660 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-027-B023	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-05-24 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-03-23 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity Tachyarrhythmia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jun-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1J243J1, SC 12000 IU weekly since 2011-May-24 for renal anemia. On 2012-Mar-23 the patient developed myocardial infarction and was hospitalised. The patient recovered and was discharged on 2012-Apr-04. Patient's medical history included tachyarrhythmia absoluta since 2010-Jul and obesity. The reporter did not assess the causal relationship between event and SILAPO. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jun-29. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-065440 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-027-B026	60 to 69	Male	SILAPO InjektionsÃ¶sung in Fertigspritze INN: epoetin zeta Start: 2011-05-23 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2013-08-25 Outcome: recovered	Ischaemic stroke / epoetin zeta: unknown	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia Renal failure Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO InjektionsÃ¶sung in Fertigspritze (INN: epoetin zeta) batch: 2N333C3, subcutaneously 4000 I.U. weekly since 2011-May-23 for renal anaemia. On 2013-Aug-25 the patient developed ischemic stroke for which he was hospitalised. The event was not resolved at the time of report. The reporter did not assess the causal relationship between suspected drug and event. Follow-up information #1 was received on 2013-Oct-01: Medical history included renal insufficiency (requiring dialysis) and diabetes mellitus type 2b. The patient was treated with intravenous systemic thrombolysis with rTPA and was discharged on 2013-Sep-03. The event resolved. The reporter assessed the causal relationship between suspected drug and event as not related. Follow-up information #2 was received on 2013-Nov-04: The event resolved on 2013-Oct-04.
DE-STADA-102585 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-029-B001	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-01-31 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2015-07-28 Outcome: recovered	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Aug-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 1000 IU weekly subcutaneously since 2015-Jan-31 for renal anemia. On 2015-Jul-30 the patient was hospitalised with syncope and developed lung embolism. The patient was reanimated and received lysis with Marcumar (INN: phenprocoumon). The event resolved. The reporter assessed the causal relationship between the event and SILAPO as possible related. Follow-up information #1 was received on 2015-Aug-31: The start of event and hospitalisation was corrected to 2015-Jul-28. The patient was discharged on 2015-Aug-28. The therapy with Silapo was continued.
DE-STADA-042776 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B005	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-04-23 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebrovascular accident Onset: 2011-10-27 Outcome: recovered	Cerebrovascular accident / epoetin zeta: not related	Cerebrovascular accident / epoetin zeta: not assessable	Cerebrovascular accident / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-Apr-23 for renal anemia. On 2011-Oct-27 the patient developed an unspecified stroke and was hospitalised. The event resolved on 2011-Nov-16 and the patient was discharged. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-069398 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B007	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-10-03 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina pectoris Onset: 2013-11-18 Outcome: recovered	Angina pectoris / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 2000 IU subcutaneously weekly since 2013-Oct-03 for renal anemia. On 2013-Nov-18 the patient was hospitalised with angina pectoris. The patient received intracardiac catheter and the event resolved. The patient was discharged on 2013-Nov-28. The reporter assessed the causal relationship between the event and SILAPO as not assessable.
DE-STADA-168128 v1.0	Yes Patient died	DE-029-B011	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2014-12-19 End: not stated Dosage: 1 x 500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac failure Onset: 2016-09-29 Outcome: fatal	Cardiac failure / epoetin zeta: unlikely related	Cardiac failure / epoetin zeta: not assessable	Cardiac failure / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Aug-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Dec-19 for renal anemia. The current SILAPO dose was 500 IU weekly. On 2016-Sep-29 the patient died at home due to heart failure. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-038612 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B015	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-05-16 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2011-09-05 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Sep-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 9M116M9, SC 4000 IU weekly since 2011-May-16 for renal anemia. On 2011-Sep-05 the patient was hospitalised due to shunt occlusion. A shunt revision was performed. The event was ongoing at the time of report. The patient's medical history included adipositas. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up #1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Sep-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. The patient was discharged on 2011-Sep-07 in good general condition.
DE-STADA-074063 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B016	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-10-03 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina pectoris Onset: 2014-01-07 Outcome: recovered with sequel Atrial fibrillation Onset: 2014-01-07 Outcome: recovered with sequel	Angina pectoris / epoetin zeta: not assessable Atrial fibrillation / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: not assessable Aerial fibrillation / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: not listed Atrial fibrillation / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Mar-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 18000 IU subcutaneously weekly since 2013-Oct-03 for renal anemia. On 2014-Jan-07 the patient was hospitalised with angina pectoris and newly occurred atrial fibrillation. The patient received anticoagulation therapy. The patient was discharged on 2014-Jan-15 and was recovered with sequelae. The dose of SILAPO was increased. The reporter assessed the causal relationship between the event and SILAPO as not assessable. Medical history incuded obesity. Follow-up information #1 was received on 2014-Sep-15: Field action taken with drug was corrected from dose not changed to dose increased.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-093327 v1.0	Yes Other medical important condition	DE-029-B018	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-10-03 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2015-01-09 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: unlikely related	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Mar-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU subcutaneously weekly since 2013-Oct-03 for renal anemia. On 2015-Jan-09 the patient developed arterial occlusive disease of the legs. The wound on foot was medically treated. At the time of report the event was not resolved. The dose of SILAPO was not changed. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Medical history incuded obesity. Cross ref.: DE-STADA-074063 (same patient).
DE-STADA-097919 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B016	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-10-03 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2015-03-05 Outcome: recovered with sequel Infected bunion Onset: 2015-03-05 Outcome: recovered with sequel	Arterial occlusive disease / epoetin zeta: not assessable Infected bunion / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not assessable Infected bunion / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not listed Infected bunion / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Jun-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU subcutaneously weekly since 2013-Oct-03 for renal anemia. On 2015-Mar-05 the patient developed infected of bunion with progressive arterial occlusive disease. The patient was hospitalised on 2015-Mar-25. The bunion was amputated and percutaneous transluminal angiography of lower leg was performed. The patient was discharged on 2015-Mar-26. The dose of SILAPO was not changed. The reporter assessed the causal relationship between the event and SILAPO as not assessable. Medical history included obesity. Cross ref.: DE-STADA-074063, DE-STADA-093327 (same patient).
DE-STADA-108040 v1.0	No	DE-029-B017	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-06-14 End: 2015-11-23 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Bone pain Onset: 2015-11-23 Outcome: recovered	Bone pain / epoetin zeta: possible related	Bone pain / epoetin zeta: possible related	Bone pain / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Dec-04 and on 2015-Dec-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2015-Jun-14 for renal anemia. On 2015-Nov-23 the patient developed bone pain on the day of Silapo administration. The patient mentioned bone pain after former Silapo administrations Silapo was withdrawn and the patient was changed to another epoetin therapy (Neo Recormon). The event resolved the same day. Medical history included obesity. The reporter assessed the causal relationship between the event and SILAPO as possible related.
DE-STADA-074067 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B020	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-02-18 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2014-02-18 Outcome: recovered with sequel	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Mar-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2013-Feb-18 for renal anemia. On 2014-Feb-18 the patient developed shunt occlusion. The patient was hospitalised and atrial catheter as dialysis access was performed. The patient was discharged on 2014-Feb-25 and was resolved with sequelae. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-122100 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B024	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-12-16 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pericardial effusion Onset: 2016-06-10 Outcome: recovered	Pericardial effusion / epoetin zeta: not assessable	Pericardial effusion / epoetin zeta: not assessable	Pericardial effusion / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Aug-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Dec-16 for renal anemia. The current dose of SILAPO was 2000 IU weekly. On 2016-Jun-10 the patient developed acute dyspnoea due to pericardial effusion. The patient was hospitalised the same day: medical therapy and shunt insertion as dialysis preparation was conducted. The patient was discharged on 2016-Jun-16. The patient recovered. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-089118 v3.0	Yes Other medical important condition	DE-029-B026	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-03-03 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2014-12-12 Outcome: recovered	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2014-Mar-03 for renal anemia. On 2014-Dec-12 the patient developed shunt occlusion. The patient was hospitalised and a new shunt was implanted. The event resolved and the patient was discharged on 2014-Dec-16. The reporter assessed the causal relationship between event and SILAPO as not assessable. Medical history included obesity. Follow-up information #1 was received on 2015-Feb-21: The therapy with SILAPO was continued. Follow-up information #2 was received on 2015-Sep-09: The date of event onset was corrected on the SAE form from 2015-Nov-12 to 2015-Dec-12.
DE-STADA-185788 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B028	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-04-16 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebrovascular accident Onset: 2019-07-01 Outcome: not recovered Peripheral swelling Onset: 2019-07-01 Outcome: not recovered	Cerebrovascular accident / epoetin zeta: not assessable Peripheral swelling / epoetin zeta: not assessable	Cerebrovascular accident / epoetin zeta: not assessable Peripheral swelling / epoetin zeta: possible related	Cerebrovascular accident / epoetin zeta: listed Peripheral swelling / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Aug-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Apr-16 for renal anemia. The current dose was 2000 IU weekly and current Batch no. 7X09808. On 2019-Jul-01 the patient was hospitalised with swelling of left arm which was not resolved at the time of report. The last administration of SILAPO prior to the event was 2019-Jun-24. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up information #1 was received on 2020-Mar-30: The patient was hospitalised with swelling of arm and apoplexy on 2019-Jul-01. The patient was discharged on 2019-Oct-03. The event was not resolved at the time of report. The SILAPO therapy was continued. The reporter assessed the causal relationship between events and SILAPO as not assessable.
DE-STADA-185786 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-029-B029	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-08-15 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2019-05-24 Outcome: fatal	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Bronchial carcinoma Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Aug-19 and on 2019-Aug-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Aug-15 for renal anemia. The current dose was 2000 IU weekly. Batch not provided. On 2019-May-24 the patient developed myocardial infarction, Despite resuscitation, the patient died. Cause of death was bronchial carcinoma and myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not assessable.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-071173 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B033	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-12-10 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	General physical health deterioration Onset: 2014-01-10 Outcome: not recovered Asthenia Onset: 2014-01-10 Outcome: not recovered Duodenal ulcer Onset: 2014-01-10 Outcome: unknown	Asthenia / epoetin zeta: not assessable Duodenal ulcer / epoetin zeta: not assessable General physical health deterioration / epoetin zeta: not assessable	Asthenia / epoetin zeta: not assessable Duodenal ulcer / epoetin zeta: unlikely related General physical health deterioration / epoetin zeta: not assessable	Asthenia / epoetin zeta: listed Duodenal ulcer / epoetin zeta: not listed General physical health deterioration / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jan-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 2000 IU subcutaneously weekly since 2013-Dec-10 for renal anemia. On 2014-Jan-10 the patient developed deterioration of general condition and asthenia and was therefore hospitalised on 2014-Jan-12. The reporter assessed the causal relationship between the event and SILAPO as not assessable. Follow-up information #1 was received on 2014-Jan-21: Also an ulcus duodeni was observed. Patient was discharged on 2014-Jan-20. The reporter assessed the causal relationship between the event and SILAPO as not assessable.
DE-STADA-111537 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B033	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-12-10 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2016-01-06 Outcome: recovered	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Feb-056. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2013-Dec-10 for renal anemia. The current dose of SILAPO was 8000 IU weekly. On 2016-Jan-06 the patient was hospitalised for shunt occlusion. A shunt revision was performed and the event resolved on 2016-Jan-08. The patient was discharged. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross ref.: DE-STADA-071173 (same patient).
DE-STADA-122095 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B033	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-12-10 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Gangrene Onset: 2016-07-06 Outcome: recovered with sequel	Gangrene / epoetin zeta: not assessable	Gangrene / epoetin zeta: not assessable	Gangrene / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Aug-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2013-Dec-10 for renal anemia. The current dose of SILAPO was 8000 IU weekly. On 2016-Jul-06 the patient developed livide discoloration of forefoot. The patient was hospitalised on 2016-Jul-20: A percutaneous transluminal angiography, stent implantation and amputation of 1. foot ray was conducted. The patient was discharged on 2016-Aug-04. The patient recovered with sequelae. The therapy with SILAPO was continued. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross ref.: DE-STADA-071173, DE-STADA-111537 (same patient).
DE-STADA-102586 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B036	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-05-23 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2015-07-21 Outcome: recovered	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Aug-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU weekly subcutaneously since 2015-May-23 for renal anemia. On 2015-Jul-21 the patient was hospitalised for shunt occlusion. A percutaneous transluminal angioplasty was performed and the event resolved on 2015-Jul-23. The patient was discharged on 2015-Jul-25. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-129623 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B036	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-05-23 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2016-09-21 Outcome: recovered	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Dec-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-23 for renal anemia. The current dose was 8000 IU weekly. On 2016-Sep-21 the patient developed transient ischemic attacks and corresponding syndromes (sensitivity disorder of right face). The patient was hospitalised on 2016-Sep-22. An apoplexy was excluded. The event resolved on 2016-Sep-24 and the patient was discharged. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross ref.: DE-STADA-102586 (same patient).
DE-STADA-152394 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B036	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-05-23 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Atrial fibrillation Onset: 2017-09-22 Outcome: recovered with sequel Palpitations Onset: 2017-09-22 Outcome: recovered	Atrial fibrillation / epoetin zeta: not assessable Palpitations / epoetin zeta: not related	Atrial fibrillation / epoetin zeta: possible related Palpitations / epoetin zeta: not related	Atrial fibrillation / epoetin zeta: not listed Palpitations / epoetin zeta: not applicable	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-23 for renal anemia. The current dose was 24000 IU weekly. On 2017-Sep-22 the patient developed heart racing and was hospitalised. Atrial fibrillation was diagnosed. The patient's medications were adapted and cardioversion was performed. The patient was discharged on 2017-Sep-28. The patient recovered with sequelae. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross ref.: DE-STADA-102586, - 129623, -152395 (same patient) Follow-up information #1 was received on 2018-Feb-16: The heart racing did not improve after change of medication. On 2017-Dec-12 the patient was hospitalised for ablation and cardiac pacemaker insertion. The event resolved and the patient was discharged on 2017-Dec-18. The therapy with SILAPO was continued. The batch of administered SILAPO product was not provided. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #2 was received on 2018-Aug-27: The batch of administered SILAPO product was provided as 7OC1807.
DE-STADA-152395 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B036	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-05-23 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt malfunction Onset: 2017-09-05 Outcome: recovered	Shunt malfunction / epoetin zeta: not related	Shunt malfunction / epoetin zeta: not assessable	Shunt malfunction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-23 for renal anemia. The current dose was 24000 IU weekly. On 2017-Sep-05 the patient developed swelling of shunt arm and development of aneurysm. The patient was hospitalised and a shunt dysfunction was diagnosed. A shunt revision was performed. The event resolved and the patient was discharged on 2017-Sep-08. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-102586, - 129623, -152394 (same patient)
DE-STADA-072054 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-029-B039	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-04-25 End: 2014-01-06 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2014-01-07 Outcome: fatal	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jan-27 and 2014-Jan-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2011-Apr-25 for renal anemia. On 2014-Jan-07 the patient was hospitalized with arterial occlusive disease of his legs, his feet showed livid discoloration. On 2014-Jan-25 the patient received bypass surgery, reanimation was needed but did not work. He died during the procedure, probably cardiac death. According to the reporter, causal relationship of the event to SILAPO was not assessable. Follow-up report #1 was generated on 2014-Feb-12 after internal case review in order to add the Sponsor's study number in the structured field.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-069371 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B043	70 to 79	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-08-28 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2013-11-10 Outcome: recovered	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 2000 IU subcutaneously weekly since 2013-Aug-28 for renal anemia. On 2013-Nov-10 the patient was hospitalised with dyspnoea and cough. A lung embolism was diagnosed and the patient received Marcumar (INN: phenprocoumon). The event resolved and the patient was discharged on 2013-Nov-22. The reporter assessed the causal relationship between the event and SILAPO as possible related.
DE-STADA-042100 v1.0	Yes Other medical important condition	DE-029-B041	50 to 59	Female	N/A	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Haemoglobin decreased Onset: 2011-12-23 Outcome: not recovered Duodenitis Onset: 2011-12-23 Outcome: not recovered Gastritis erosive Onset: 2011-12-23 Outcome: not recovered Haemorrhagic anaemia Onset: 2011-12-23 Outcome: not recovered	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) SC 4000 IU weekly since 2011-Sep-27 for renal anemia. On 2011-Dec-23 the patient developed erosive gastritis and duodenitis with blood loss anemia and hemoglobin decrease. The pateint was treated with a high dose proton-pump inhibitor therapy, intravenous iron and increase in SILAPO dosage. At the time of report the patient was not recovered. The report assessed the causal relationship to SILAPO as not related.
DE-STADA-054761 v5.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B041	50 to 59	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2011-09-27 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2012-11-02 Outcome: recovered Shunt occlusion Onset: 2014-05-17 Outcome: recovered Shunt occlusion Onset: 2013-12-23 Outcome: recovered	Shunt occlusion / epoetin zeta: not assessable Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) SC 12000 IU weekly since 2011-Sep-27 for renal anemia. On 2012-Nov-02 the patient developed shunt occlusion and was hospitalised. Shunt revision and an implantation of Goretex Loop was performed. The event resolved on 2012-Nov-08 and the patient was discharged on 2012-Nov-19. The reporter assessed the causal relationship to SILAPO as possible related. Cross reference: DE-STADA-042100 (same patient). Follow-up information #1 was received on 2013-Mar-01: The patient again developed shunt occlusion on 2012-Dec-13 which resolved on 2012-Dec-19 and on 2013-Jan-18 which resolved at the same day. Follow-up information #2 was received on 2013-Dec-30: The dose of SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) was reduced to 10000 IU subcutaneously weekly. The patient again developed shunt occlusion on 2013-Dec-23 which resolved on 2013-Dec-27. The reporter assessed the causal relationship to SILAPO as not assessable. Follow-up information #3 was received on 2014-May-28: The dose of SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) was reduced to 8000 IU subcutaneously weekly. The patient again developed shunt occlusion on 2014-May-17 and was hospitalised. A shunt revision was performed and the event resolved on 2014-May-22. The patient was discharged the same day. The reporter assessed the causal relationship to SILAPO as not assessable. Follow-up information # was received on 2014-Sep-15: The reaction stop date for shunt occlusion occurred on 2014-May-17 was reported to be the 2014-May-21 instead 2014-May-22 as previously reported.
DE-STADA-146350 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B042	70 to 79	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2015-09-22 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Atrial fibrillation Onset: 2016-07-12 Outcome: not recovered	Atrial fibrillation / epoetin zeta: not assessable	Atrial fibrillation / epoetin zeta: not assessable	Atrial fibrillation / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Sep-22 for renal anemia. The current dose was 6000 IU weekly. On 2016-Jul-12 the patient developed atrial fibrillation and was hospitalised. An anticoagulation therapy was performed. The patient was discharged on 2016-Jul-26. The event was not resolved at the time of report. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-093323 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B045	70 to 79	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-06-28 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2014-09-04 Outcome: recovered	Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Mar-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 1000 IU weekly subcutaneously since 2013-Jun-28 for renal anemia. On 2014-Sep-04 the patient developed shunt dysfunction and was hospitalised. A percutaneous transluminal angioplasty for stenosis of vena basilica and vena subclavia was performed. The event resolved on 2014-Sep-05 and the patient was discharged. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-097915 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B045	70 to 79	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2013-06-28 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt stenosis Onset: 2015-03-10 Outcome: recovered	Shunt stenosis / epoetin zeta: unlikely related	Shunt stenosis / epoetin zeta: not assessable	Shunt stenosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Jun-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2013-Jun-28 for renal anemia. On 2015-Mar-10 the patient developed shunt stenosis and was hospitalised. A shunt dilatation was performed. The event resolved and the patient was discharged on 2015-Mar-12. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-093323 (same patient).
DE-STADA-194895 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B047	60 to 69	Female	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2017-07-07 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2019-11-15 Outcome: recovered Wound Onset: 2019-11-15 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: not related Wound / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable Wound / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed Wound / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-Feb-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female obese patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Jul-07 for renal anemia. The current dose of SILAPO was 12000 IU weekly. Batch number not known. On 2019-Nov-15 the patient was hospitalised due to a wound at the lower leg with assumed arterial occlusion disease. On 2019-Nov-23 the patient was discharged without sequelae. The last administration of SILAPO prior onset was 2019-Nov-13. The therapy with SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-053728 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B048	80 to 89	Male	SILAPO Injektionslsoesung in Fertigspritze INN: epoetin zeta Start: 2012-05-21 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt stenosis Onset: 2012-08-10 Outcome: recovered	Shunt stenosis / epoetin zeta: not related	Shunt stenosis / epoetin zeta: not assessable	Shunt stenosis / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Nov-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslsoesung in Fertigspritze (INN: epoetin zeta) subcutaneously 18000 IE weekly since 2012-May-21 for renal anemia. On 2012-Aug-10 the patient developed shunt stenosis. The patient underwent percutaneous transluminal angioplasty and recovered on 2012-Aug-10. The patient was discharged on 2012-Aug-15. The SILAPO dose was increased. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up report #1 was generated on 2012-Dec-11 after internal case review in order to correct the gender of the patient from female to male.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-054757 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B048	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-05-21 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Hypoglycaemia Onset: 2012-11-29 Outcome: recovered	Hypoglycaemia / epoetin zeta: not assessable	Hypoglycaemia / epoetin zeta: unlikely related	Hypoglycaemia / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously 12000 IE weekly since 2012-May-21 for renal anemia. On 2012-Nov-29 the patient was hospitalised with somnolence due to hypoglycemia. The event resolved. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross reference: DE-STADA-053728 (same patient). Follow-up information #1 was received on 2013-Apr-29: The event resolved on 2012-Dec-03.
DE-STADA-084280 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B049	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-03-17 End: 2014-07-07 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2014-07-12 Outcome: recovered	Deep vein thrombosis / epoetin zeta: possible related	Deep vein thrombosis / epoetin zeta: possible related	Deep vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Sep-16. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2014-Mar-17 for renal anemia. On 2014-Jul-12 the patient developed deep vein thrombosis of the lower limbs. The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-069397 v1.0	Yes Other medical important condition	DE-029-B050	40 to 49	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-07-11 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Delusion Onset: 2013-10-18 Outcome: recovered	Delusion / epoetin zeta: not assessable	Delusion / epoetin zeta: not related	Delusion / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 12000 IU subcutaneously weekly since 2011-Jul-11 for renal anemia. On 2013-Oct-18 the patient presented with hallucination and delusion on psychiatric unit. The patient was regulated with medication and the event resolved on 2013-Oct-20. The reporter assessed the causal relationship between the event and SILAPO as not assessable.
DE-STADA-084228 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B050	40 to 49	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-07-11 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2014-01-27 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Sep-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2011-Jul-11 for renal anemia. On 2014-Jan-27 he was hospitalised for examination for pain in his feet. An angiography was performed and arterial occlusive disease was diagnosed. On 2014-Jan-29 the patient was discharged. The outcome was reported to be still present and permanent harm was described. According to the reporter, causal relationship of the event to SILAPO was not assessable.
DE-STADA-046897 v3.0	Yes Patient died Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B053	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-04-02 End: 2014-01-06 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2012-04-16 Outcome: recovered Death Onset: 2014-01-13 Outcome: fatal	Death / epoetin zeta: not assessable Ischaemic stroke / epoetin zeta: unlikely related	Death / epoetin zeta: not assessable Ischaemic stroke / epoetin zeta: not assessable	Death / epoetin zeta: not listed Ischaemic stroke / epoetin zeta: listed	Arrhythmia Dialysis Hypertension Nephrogenic anaemia Obesity Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-May-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), batch: 1J243J1, SC 6000 IU weekly since 2012-Apr-02 for renal anemia. On 2012-Apr-16 the patient developed an ischemic stroke and was hospitalised. A carotis thrombo-endarterectomy was performed and the patient was discharged on 2012-May-03. The event involved persistence of significant disability and was reported to be not recovered. The therapy with SILAPO was discontinued on 2012-Apr-16. Medical history included arrhythmia, hypertension, adipositas and dialysis dependent renal insufficiency. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-05. After the ischemic stroke the therapy with SILAPO was discontinued in the hospital but was later reintroduced in the dialysis centre. The patient was doing well. Follow-up#2 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jan-21. The patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 8000 IU weekly. The patient was found dead at home on 2014-Jan-13. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-123944 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B058	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-02-11 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2016-08-25 Outcome: not recovered Anaemia of malignant disease Onset: 2016-08-25 Outcome: not recovered	Anaemia of malignant disease / epoetin zeta: unlikely related Drug ineffective / epoetin zeta: unlikely related	Anaemia of malignant disease / epoetin zeta: unlikely related Drug ineffective / epoetin zeta: unlikely related	Anaemia of malignant disease / epoetin zeta: listed Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia Prostate cancer metastatic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Sep-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 240000 IU weekly subcutaneously since 2015-Feb-11 for renal anemia. On 2016-Aug-25 a severe anemia was detected and lack of drug effect was noted. The patient was hospitalised and received transfusion of 2 erythrocytes concentrates. The patient was discharged on 2016-Sep-01 and SILAPO dose was increased. The event was not resolved at the time of report. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up information #1 was received on 2016-Sep-28: The patient suffered from severe cancer anemia in osseous metastatic prostate cancer. According to the physician the anemia at the current stage could not be controlled by SILAPO alone. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #2 was received on 2016-Dec-15: The patient died due to metastatic prostate cancer on 2016-Oct-04.
DE-STADA-084218 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-029-B059	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-05-05 End: 2014-05-28 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Abdominal hernia Onset: 2014-05-28 Outcome: not recovered Peritonitis bacterial Onset: not stated Outcome: fatal	Abdominal hernia / epoetin zeta: unlikely related Peritonitis bacterial / epoetin zeta: unlikely related	Abdominal hernia / epoetin zeta: unlikely related Peritonitis bacterial / epoetin zeta: unlikely related	Abdominal hernia / epoetin zeta: not listed Peritonitis bacterial / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Sep-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 12000 IU intravenously weekly since 2014-May-05 until 2014-May-28 for renal anemia. On 2014-May-28 the patient was hospitalised due to an Abdominal hernia, during the further course the patient developed Peritonitis bacterial and subsequentially died. The reporter assessed the causal relationship between the event and SILAPO as unlikely.
DE-STADA-069394 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-029-B062	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-06-23 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2013-08-08 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 6000 IU subcutaneously weekly since 2011-Jun-23 for renal anemia. On 2013-Aug-08 the patient suffered from persisting infection of big toe. The patient was hospitalised on 2013-Sep-18 and peripheral arterial disease stage IV was diagnosed. The toe was amputated and the patient was discharged on 2013-Sep-24. The reporter assessed the causal relationship between the event and SILAPO as not assessable. Medical history included obesity.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-068959 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B070	70 to 79	Male	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Subdural haematoma Onset: 2013-10-30 Outcome: recovered with sequel	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 24000 IU subcutaneously weekly since 2011-Aug-12 for renal anemia. On 2013-Oct-30 the patient developed subdural haematoma described as behavioral changes and fall. The event resolved on 2013-Nov-11 with sequelae. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-129622 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B071	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-08-19 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2016-10-01 Outcome: recovered	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Dec-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Aug-19 for renal anemia. The current dose was 2000 IU weekly. The patient was hospitalised on 2016-Oct-01 due to left thoracic pain. Unstable angina pectoris was detected. The event resolved on 2016-Oct-06 and the patient was discharged. Last SILAPO administration prior onset was 2016-Sep-27. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up information #1 was received on 2017-Sep-08: SILAPO dosage was corrected to 1 x 4000 IU per week.
DE-STADA-152398 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B071	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-08-19 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Bladder neoplasm Onset: 2017-09-11 Outcome: not recovered Haematuria Onset: 2017-09-01 Outcome: not recovered	Bladder neoplasm / epoetin zeta: not assessable Haematuria / epoetin zeta: not assessable	Bladder neoplasm / epoetin zeta: not assessable Haematuria / epoetin zeta: not assessable	Bladder neoplasm / epoetin zeta: not listed Haematuria / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Aug-19 for renal anemia. The current dose was 6000 IU weekly. On 2017-Sep-11 a macrohematuria was detected which led to the diagnosis bladder tumour. A tumour resection was scheduled. The event was not resolved at the time of report. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Cross ref.: DE-STADA-129622 (same patient) Follow-up information #1 was received on 2018-Feb-16 and on 2018-Feb-20: The macrohaematuria was detected on 2017-Sep-01. From 2017-Dec-13 to 2017-Dec-16 the patient was again hospitalised for transurethral bladder resection. The event was not yet resolved at the time of report. The current dose of SILAPO was 12000 IU weekly and was continued. Follow-up information #2 was received on 2018-Feb-27: The batch of the currently administered SILAPO was 70027P7.
DE-STADA-065240 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-029-B073	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-07-08 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pneumonia Onset: 2013-08-22 Outcome: recovered with sequel	Pneumonia / epoetin zeta: not assessable	Pneumonia / epoetin zeta: unlikely related	Pneumonia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Aug-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 I.E. weekly subcutaneously since 2013-Jul-08 for renal anemia. On 2013-Aug-23 the patient was hospitalised due to a fall caused by pneumonia on 2013-Aug-22. The pneumonia was treated with antibiotics and was not resolved at the time of report. The reporter assessed the causal relationship between event and SILAPO as not assessable. Follow-up #1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. The patient was discharged on 2013-Sep-11. The outcome was reported to be recovered with sequel. Additional serious criteria life-threatening was ticked.
DE-STADA-167642 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-029-B074	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2017-04-17 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt stenosis Onset: 2018-06-19 Outcome: recovered	Shunt stenosis / epoetin zeta: unlikely related	Shunt stenosis / epoetin zeta: not assessable	Shunt stenosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Aug-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin eta) subcutaneously since 2017-Apr-17 for renal anemia. The current dose of SILAPO was 18000 IU weekly. Batch not provided. On 2018-Jun-19 the patient developed shunt stenosis and was hospitalised on 2018-Jun-26 for shunt revision. The event resolved the same day and the patient was discharged on 2018-Jul-09. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-042783 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-030-B004	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-04-25 End: 2011-12-05 Dosage: 2 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2011-12-08 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Aortic valve replacement Atrial fibrillation Hyperlipidaemia Hypertension Nephrogenic anaemia Obesity Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 6000 IU weekly since 2011-Apr-25 for renal anemia. On 2011-Dec-09 the patient developed an apoplexy and was hospitalised. Medical history included hyperlipidemia, hypertension, diabetes type 2 and atrial fibrillation. No further information was provided. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jan-23. The dosage of SILAPO was corrected to SC 6000 IU twice weekly and batch no was OM203C1. The patient developed apoplexy on 2011-Dec-08 and not on 2011-Dec-09 as previously reported. Further medical history included condition after aortic valve replacement in 1997 and obesity. The reporter assessed the causal relationship between the event and therapy with SILAPO as unlikely related. Follow-up#2 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-23. The event was now reported as ischaemic stroke, not -as previously reported - as apoplexy. The last administration before onset was 2011-Dec-05. SILAPO Injektionsloesung in Fertigspritze was withdrawn after the event. The outcome was reported to be recovered with sequel. The patient was discharged on 2012-Feb-09. The reporter assessed the causal relationship between suspected drug and event as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-108115 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B001	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-03-24 End: not stated Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2016-11-22 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Dec-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously, 3000 IU weekly since 2015-Mar-24 for renal anemia. On an unspecified date the patient developed peripheral arterial occlusive disease. The event was treated with conservative therapy. At the time of report the event was not yet resolved. The dose of SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2020-May-28: The SILAPO dose was corrected to 5000 IU weekly and the last administration of SILAPO prior to the event was on 2016-Nov-19. The event was corrected to arterial occlusion at known peripheral arterial occlusive disease. Start date of event was 2016-Nov-22. The patient was hospitalised on 2016-Nov-22 and treated conservatively. Patient was discharged on 2016-Nov-23. The event was not resolved. Batch number could not be obtained.
DE-STADA-049973 v1.0	Yes Patient died	DE-033-B003	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-09-10 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac death Onset: 2012-07-12 Outcome: fatal	Cardiac death / epoetin zeta: not related	Cardiac death / epoetin zeta: not assessable	Cardiac death / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2011-Sep-10 for renal anemia. On 2012-Jul-12 the patient died due to cardiac cause (not specified). The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-123933 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-033-B008	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-11-25 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-04-04 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Sep-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 15000 IU weekly subcutaneously since 2015-Nov-25 for renal anemia. On 2016-Apr-04 the patient was hospitalised with myocardial infarction confirmed by coronary angiography. The patient underwent bypass surgery. The event resolved on 2016-Apr-08 and the patient was discharged on 2016-Apr-21. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-072934 v5.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-033-B010	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-11-16 End: not stated Dosage: 1 x 2500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2014-01-25 Outcome: unknown Arterial occlusive disease Onset: 2014-11-12 Outcome: recovered Extremity necrosis Onset: 2014-11-12 Outcome: recovered Vascular graft complication Onset: 2014-04-26 Outcome: recovered with sequel Wound Onset: 2014-01-25 Outcome: unknown	Arterial occlusive disease / epoetin zeta: not related Extremity necrosis / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not related Vascular graft complication / epoetin zeta: not related Wound / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not related Extremity necrosis / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not assessable Vascular graft complication / epoetin zeta: not related Wound / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not listed Extremity necrosis / epoetin zeta: not listed Peripheral arterial occlusive disease / epoetin zeta: not listed Vascular graft complication / epoetin zeta: not listed Wound / epoetin zeta: not listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU subcutaneously weekly since 2013-Nov-16 for renal anemia. On 2014-Jan-25 the patient was hospitalised with deterioration of a preexisting peripheral arterial disease with open wound on left foot. A peripheral bypass surgery was performed. The outcome of the event was unknown. The reporter assessed the causal relationship between the event and SILAPO as not related. Follow-up information #1 was received on 2014-Apr-16: The patient was discharged on 2014-Mar-08. The outcome of the event was not reported. Follow-up information #2 was received on 2014-May-16: At the time of report the patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 15000 IU subcutaneously weekly. On 2014-Apr-26 the patient developed occlusion of popliteo-pedal bypass. The patient underwent amputation of left thigh. The reporter assessed the causal relationship between the event and SILAPO as not related. Follow-up information #3 was received on 2014-Nov-24: The patient was discharged on 2014-Jun-12 Follow-up information #4 was received on 2015-Feb-24: At the time of report the patient received 2500 IU SILAPO weekly. On 2014-Nov-12 the patient developed occlusion of arteria femoralis communis left with thigh stump necrosis and was hospitalised. In hospital the patient underwent revascularisation of arteria femoralis. The event resolved on 2014-Dec-12 and the patient was discharged on 2014-Dec-23. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-057216 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B011	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-08-29 End: not stated Dosage: 1 x 25000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-11-16 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Diabetes mellitus Hypertensive heart disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Feb-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 25000 I.E. weekly subcutaneously since 2011-Aug-29 for renal anemia. On 2012-Nov-16 the patient was hospitalised with myocardial infarction. The event was treated with percutaneous transluminal angioplasty and stent insertion. The event resolved on 2012-Nov-16 and the patient was discharged on 2012-Dec-03. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history inlcuded preexisting hypertensive heart disease and diabetes.
DE-STADA-079672 v2.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-033-B012	30 to 39	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-11-14 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Renal artery thrombosis Onset: 2014-05-14 Outcome: recovered with sequel	Renal artery thrombosis / epoetin zeta: unlikely related	Renal artery thrombosis / epoetin zeta: not assessable	Renal artery thrombosis / epoetin zeta: listed	Nephrogenic anaemia Renal transplant	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jun-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient has been receiving SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2012-Nov-14 for renal anemia. The patient was hospitalised on 2014-May-14 due to partial thrombosis of the artery of her transplanted kidney, which caused partial loss of renal transplant function (Renal artery thrombosis). Patient was released on 2014-Jun-17. Follow-up information #1 was received on 2014-Nov-24: SILAPO was administered 10 000 IU weekly subcutaneously and the therapy was continued. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-085272 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B014	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2014-01-17 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral artery stenosis Onset: 2014-08-20 Outcome: recovered	Peripheral artery stenosis / epoetin zeta: not related	Peripheral artery stenosis / epoetin zeta: not assessable	Peripheral artery stenosis / epoetin zeta: listed	Arteriosclerosis Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Oct-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 15000 IU weekly subcutaneously since 2014-Jan-17 for renal anemia. The patient was hospitalised on 2014-Aug-12. On 2014-Aug-20 the patient developed recurrent stenosis of right leg arteries and underwent percutaneous transluminal angioplasty and stent insertion. The event resolved and the patient was discharged on 2014-Sep-22. Medical history included known vasosclerosis. The reporter assessed the causal relationship between the event and SILAPO as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-088300 v3.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-033-B023	60 to 69	Female	SILAPO InjektionsÃ¶sung in Fertigspritze INN: epoetin zeta Start: 2014-10-29 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2014-11-27 Outcome: unknown	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient started receiving SILAPO InjektionsÃ¶sung in Fertigspritze (INN: epoetin zeta) 5000 I.U weekly for renal anaemia on 2014-Oct-29. Last administration prior event onset was 2014-Nov-26. On 2014- Nov-27 the patient suffered from ischaemic stroke. The patient was hospitalised due to the event the same day. The event was still present. Patient's medical history included ongoing type 2 diabetes mellitus. The reporter assessed the causal relationship between suspected drug and event as unlikely related. Follow-up information #1 was received on 2015-Jan-08 and 2015-Jan-09. The ischemic stroke was described as middle cerebral artery infarction right, patent Foramen ovale with atrial septal defect and paradoxical embolism. The patient was discharged on 2015-Jan-04. The outcome of the event was unknown. SILAPO therapy was not changed. Follow-up information #2 was received on 2015-Dec-09: The dose of Silapo was corrected to 10000 IU per week.
DE-STADA-059438 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B027	40 to 49	Male	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: 2013-02-06 Outcome: unknown Haemoglobin decreased Onset: 2013-02-06 Outcome: recovered	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Apr-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 15000 IU weekly since 2013-Jan-09 for renal anemia. On 2013-Feb-06 a hemoglobin decrease was noticed (lack of drug effect). The patient was hospitalised on 2013-Mar-20 and a gastrointestinal bleeding was detected. The patient received medical treatment. The event resolved on 2013-Mar-26 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-062059 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-033-B027	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-01-09 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-04-15 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Hypertension Myocardial infarction Nephrogenic anaemia Obesity Type 1 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013- Jun-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 15000 IU weekly since 2013-Jan-09 for renal anemia. On 2013-Apr-15 the patient developed myocardial infarction and was hospitalised. The patient underwent percutaneous transluminal coronary angioplasty (PTCA) and stent implant. The event resolved and the patient was discharged on 2013-Ap-16. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included adipositas, diabetes mellitus type I, hypertension, coronary heart disease and condition after myocardial infarction. Cross ref.: DE-STADA-059438 (same patient).
DE-STADA-040688 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B031	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-07-18 End: 2011-10-14 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2011-10-20 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Nov-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1F221H1, SC 4000 IU weekly from 2011-Jul-18 to 2011-Oct-14 for renal anemia. On 2011-Oct-20 the patient developed myocardial infarction which required percutaneous transluminal angioplasty and stent implantation. Patient's medical history included coronary heart disease. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-045775 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B031	40 to 49	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-07-18 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2012-03-23 Outcome: not recovered Arterial occlusive disease Onset: 2012-03-23 Outcome: not recovered Femoral arterial stenosis Onset: 2012-03-23 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: not related Femoral arterial stenosis / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not assessable Femoral arterial stenosis / epoetin zeta: not assessable Peripheral arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: listed Femoral arterial stenosis / epoetin zeta: listed Peripheral arterial occlusive disease / epoetin zeta: listed	Arteriosclerosis Coronary artery disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Apr-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1J242J1, SC 2000 IU weekly since 2011-Jul-18 for renal anemia. On 2012-Mar-23 the patient developed peripheral arterial occlusive disease with high-grade stenosis of femoral artery and occlusion of 2 lower leg arteries. The patient was hospitalised and percutaneous transluminal angioplasty, stent implantation and urokinase lysis therapy was performed. At the time of report the events were not resolved. Patient's medical history included coronary heart disease and generalised arteriosclerosis. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-040688, same patient
DE-STADA-072891 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-033-B032	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-06-14 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2014-02-04 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014- Feb-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 3000 IU subcutaneously weekly since 2011-Jun-14 for renal anemia. On 2014-Feb-04 the patient was hospitalised with unstable angina pectoris. The patient underwent conservative therapy and was discharged the same day. The event resolved on 2014-Feb-06. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Follow-up information #1 was received on 2014-Apr-16: The patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU subcutaneously. The event resolved on 2014-Feb-06 and the patient was discharged the same day.
DE-STADA-043818 v2.0	Yes Other medical important condition	DE-033-B033	70 to 79	Male	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: 2012-02-02 Outcome: not recovered	N/A	N/A	N/A	Myeloproliferative disorder Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012- Feb-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 15000 IU weekly from 2011-Aug-18 for renal anemia. On 2012-Feb-02 a dose escalation with SILAPO was necessary due to lack of drug effect at known myeloproliferative syndrome. The reporter assessed the causal relationship between event and SILAPO as not related. No further information was provided. Follow-up#1 report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Apr-17. The patient's medical history included also myeloproliferative syndrome which was suspected as the cause of hemoglobin decrease. The therapy with SILAPO was continued (16000 I.U. per week at the time of report).
DE-STADA-123932 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-033-B039	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-09-12 End: 2016-07-04 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-07-04 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Arteriosclerosis Coronary artery disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016- Sep-12 and on 2016-Sep-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2015-Sep-12 for renal anemia. On 2016-Jul-04 the patient developed acute coronary syndrome (myocardial infarction) and was hospitalised. The patient underwent bypass surgery. The patient died on 2016-Jul-11 due to coronary heart disease. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease and generalised arteriosclerosis.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-076808 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-034-B010	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-10-24 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2014-03-31 Outcome: unknown	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery disease Factor XIII deficiency Hyperkalaemia Hypertension Metabolic acidosis Nephrogenic anaemia Obesity Rheumatoid arthritis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jun-03 and on 2014-Jun-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2011-Oct-24 for renal anemia. On 2014-Mar-31 the patient complained of persisting diarrhoea, angina pectoris disorder and increasing dyspnoea. The patient was hospitalised on 2014-Apr-01 and myocardial infarction was diagnosed. The patient was discharged on 2014-Apr-15 in stable general condition for further outpatient care. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease, hyperkalaemia, metabolic acidosis, atrial fibrillation, rheumatoid arthritis, hypertension, adipositas and factor 13 deficiency.
DE-STADA-074119 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-034-B011	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-01 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-12-16 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Diabetes mellitus Hypertension Nephrogenic anaemia Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Mar-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2012-Feb-01 for renal anemia. On 2013-Dec-13 the patient developed myocardial infarction. The patient was hospitalised on 2013-Dec-19 and received conservative drug therapy. The patient was discharged on 2014-Jan-17 and recovered with sequelae. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease, diabetes mellitus, hypertension and tobacco abuse. Follow-up information #1 was received on 2018-Sep-14: The dose of SILAPO was corrected to 1000 IU weekly. The last administration of SILAPO prior to the event was 2013-Sep-12.
DE-STADA-050530 v2.0	Yes Patient died	DE-034-B013	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-07-18 End: 2011-09-23 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Death Onset: 2011-10-01 Outcome: fatal	Death / epoetin zeta: unlikely related	Death / epoetin zeta: not assessable	Death / epoetin zeta: not listed	Alcohol abuse Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Aug-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 6000 IU weekly since 2011-Jul-18 for renal anemia. On 2011-Oct-01 the patient deceased. The cause of death was unknown. Patient's medical history included alcohol consumption. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2012-Aug-16: The cause of death could not be determined. The patient was found death in his flat. No autopsy was performed.
DE-STADA-072969 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-035-B072	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-08-12 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-07-29 Outcome: unknown	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2011-Aug-12 for renal anemia. On 2013-Jul-29 the patient developed myocardial infarction during a holiday and was hospitalised. The outcome of the event was unknown. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2015-Jan-12: The administered dose of SILAPO was 2000 IU weekly. The last administration of SILAPO before event was 2013-Jun-10. No further information was provided.
DE-STADA-050310 v1.0	Yes Patient died	DE-037-B001	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-17 End: 2012-07-18 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-07-18 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Aug-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1M256C2, SC 2000 IU weekly since 2012-Feb-17 for renal anemia. On 2012-Jul-18 the patient collapsed at home and was unsuccessful reanimated by emergency. The patient died due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-049116 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B004	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-11 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2012-02-18 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not listed	Gastrointestinal angiodysplasia haemorrhagic Haemodialysis Hyperlipidaemia Hyperuricaemia Nephrogenic anaemia Renal failure chronic Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-04 and on 2012-Jul-05 respectively. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1J24Z31, subcutaneous, 4000 IU weekly since 2012-Feb-11 for renal anemia. On 2012-Feb-18 the patient developed peripheral arterial occlusive disease and was hospitalised. The patient underwent percutaneous transluminal angioplasty of external iliac artery and implantation of femoro-popliteral III bypass right. The patient recovered and was discharged on 2012-Mar-14. Patient's medical hisotry included excessive smoking. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included chronic renal insufficiency, hemodialysis since 2005, hyperuricemia, hyperlipidemia and multiple angiodysplasia of stomach.
DE-STADA-088875 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B004	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-11 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2014-07-05 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Haemodialysis Lumbar spinal stenosis Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-10 and 2014-Dec-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 3T014W3, subcutaneous, 8000 IU weekly since 2012-Feb-11 for renal anemia. On 2014-Jul-05 the patient developed peripheral arterial occlusive disease and was hospitalised. The patient underwent implantation of femoro-popliteral III bypass left and thrombo-endarterectomy left. The event resolved on 2014-Jul-30 and the patient was discharged. The dose of SILAPO was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included severe tobacco abuse, preexisting peripheral arterial occlusive disease, renal insufficiency, hemodialysis and spinal canal stenosis. Cross ref.: DE-STADA-049116 (same patient)

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-054982 v4.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-037-B005	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-17 End: not stated Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2012-08-16 Outcome: recovered with sequel Peripheral ischaemia Onset: 2013-05-08 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: unlikely related Peripheral ischaemia / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable Peripheral ischaemia / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: listed Peripheral ischaemia / epoetin zeta: not listed	Angiosclerosis Arteriosclerosis Atrial fibrillation Breast cancer Glomerulonephritis Metastases to liver Nephrogenic anaemia Renal failure Renal transplant	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1N259C2, subcutaneous, 15000 IU weekly since 2012-Feb-17 for renal anemia. On 2012-Aug-16 the patient developed peripheral arterial occlusive disease stage III right tigh and was hospitalised. The patient underwent digital subtraction angiographyography, thrombo-endarterectomy and patchplastic of arteria femoralis. The event involved persistence of significant disability or incapacity. The patient was discharged on 2012-Aug-28. Medical history included severe vascular sclerosis, renal insufficiency, renal transplant March 1997, hepatic metasteses at breast cancer. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information was received the same day (2012-Dec-14): On 2012-Nov-13 the patient developed peripheral arterial occlusive disease stage IV. At the time of the event the patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 2E270F2. The patient was hospitalised on 2012-Nov-13. A recanalisation and stent implant was performed. The event involved persistence of significant disability or incapacity. The patient was discharged on 2012-Dec-04. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-054988 (same patient) Follow-up information #1 was received on 2013-Jun-13: The patient's medical history included severe angiosclerosis since December 2003. Follow-up information was received the same day (2013-Jun-13): On 2013-Jan-31 the patient developed again occlusion of arteria femoralis in the area of implanted stent as late complication after last intervention in November 2012. The patient again underwent lysis therapy and stent implant. The event resolved and the patient was discharged on 2013-Feb-02. Follow-up information was received the same day (2013-Jun-13): On 2013-May-08 the patient's condition again worsened. The patient developed again ischemia of right leg. The event was not resolved at the time of report. Follow-up information #2 was received on 2013-Jun-14: Hospital letter received. Further medical history included glomerulonephritis and atrial fibrillation. Follow-up information #3 was received on 2013-Dec-02: The patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 2J303J2, subcutaneous, 5000 IU weekly. The patient was hospitalised on 2013-Jun-13 and underwent multiple angiologic and surgical therapies with finally leg amputation. The patient was discharged on 2013-Aug-20. The dose of SILAPO was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-054988 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B005	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-17 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2012-10-09 Outcome: recovered Angina unstable Onset: 2012-10-10 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related Shunt occlusion / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable Shunt occlusion / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed Shunt occlusion / epoetin zeta: listed	Breast cancer Metastases to liver Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 2E270F2, subcutaneous, 15000 IU weekly since 2012-Feb-17 for renal anemia. On 2012-Oct-08 the patient was hospitalised for transarterial chemoembolisation. On 2012-Oct-09 the patient developed shunt occlusion which was treated by shunt revision and patch plastic and resolved. On 2012-Oct-10 the patient developed instable angina pectoris which spontaneously resolved. The patient was discharged on 2012-Oct-11. Medical history included renal insufficiency and hepatic metasteses at breast cancer. The reporter assessed the causal relationship between the events and SILAPO as unlikely related. Cross ref.: DE-STADA-054982 (same patient).
DE-STADA-050163 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B006	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-07 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2012-07-30 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: listed	Angioplasty Hypertension Nephrogenic anaemia Prostatic operation Renal aneurysm Renal failure Vascular graft	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 1M250N1, subcutaneous, 4000 IU weekly since 2012-Feb-07 for renal anemia. On 2012-Jul-30 the patient developed increased complaints with known peripheral arterial occlusive disease and was hospitalised. The patient underwent diagnostic and revascularisation therapy during hospitalisation. At the time of report the patient was not recovered. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2012-Dec-06: As treatment for the event the patient underwent femorocrural vein bypass on 2012-Aug-01. The event resolved on 2012-Aug-11 and the patient was discharged. Follow-up information #2 was received on 2012-Dec-17: Patient's medical history included intrarenale aortic aneurysm, renal insufficiency, hypertension, condition after prostatic operation and condition after various bypass procedures and percutaneous transluminal angioplasty.
DE-STADA-088869 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B006	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-07 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Haemoglobin decreased Onset: 2014-04 Outcome: recovered Angina unstable Onset: 2014-04-16 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related Haemoglobin decreased / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: unlikely related Haemoglobin decreased / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not listed Haemoglobin decreased / epoetin zeta: listed	Aortic valve stenosis Cardiac failure Dyspnoea Emphysema Haemodialysis Hyperparathyroidism secondary Nephrogenic anaemia Renal aneurysm Renal failure chronic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-10 and 2014-Dec-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 2N334C3, subcutaneously, 15000 IU weekly since 2012-Feb-07 for renal anemia. On 2014-Apr-16 the patient developed unstable angina pectoris at two-vessel coronary artery disease and aortic stenosis grade 3, additionally triggered by hemoglobin decrease to 6.9 g/dl in April 2014. The patient was hospitalised and underwent stent insertion, insertion of aortic valve prosthesis and pacemaker. Furthermore the patient received erythrocytes concentrates. The events resolved and the patient was discharged on 2014-May-26. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included aortic valve stenosis since 2013-Sep, dyspnoea, lung emphysema, chronic heart insufficiency, intrarenale aortic aneurysma, chronic renal insufficiency, haemodialysis since 2011-Apr and secondary hyperparathyroidism. Cross ref.: DE-STADA-050163 (same patient)
DE-STADA-088873 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-037-B006	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-07 End: not stated Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2014-09-02 Outcome: not recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Aortic valve replacement Cardiac pacemaker insertion Carotid artery stenosis Coronary artery disease Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure Vascular graft	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-10 and 2014-Dec-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 4S027S4, subcutaneously, 5000 IU weekly since 2012-Feb-07 for renal anemia. On 2014-Sep-02 the patient developed deterioration of preexisting peripheral peripheral artery occlusive disease grade IV. The patient was hospitalised and underwent amputation of toe on 2014-Sep-05. The patient was discharged on 2014-Sep-08. The event had not resolved. The dose of SILAPO was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included peripheral arterial occlusive disease since April 2004, asymptomatic stenosis of arteria carotis, bypass insertion, coronary heart disease, aortic valve prosthesis, pacemaker insertion, hypertension and dialysis dependent renal insufficiency. Cross ref.: DE-STADA-050163 and DE-STADA-088869 (same patient) Further information received on 2014-Dec-10: On 2014-Oct-10 the patient still suffered from persisting rest pain due to peripheral arterial occlusive disease. The patient was hospitalised and underwent transmetatarsal reamputation on 2014-Oct-15. The patient was discharged on 2014-Oct-22. The event had not resolved.
DE-STADA-062024 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-037-B007	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-02-15 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-03-17 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Delirium Hyperlipidaemia Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Pulmonary oedema Renal failure chronic Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Jun-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 I.E. weekly subcutaneously since 2012-Feb-15 for renal anemia. On 2013-Mar-17 the patient developed myocardial infarction and was hospitalised. The patient underwent reanimation and intensive care. The event resolved and the patient was discharged on 2013-Apr-18. The dosage of SILAPO was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history inlcuded tobacco abuse and pre-lung edema in December 2012 at severe hypertension. Further information received on 2013-Jun-14 (hospital letter): Further patient's medical history included chronic renal insufficiency, secondary hyperparathyroidism, hyperlipoproteinemia and delirium.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-054989 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B009	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-17 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Mesenteric artery stenosis Onset: 2012-06-25 Outcome: recovered Colitis ischaemic Onset: 2012-06-25 Outcome: recovered Gastrointestinal haemorrhage Onset: 2012-06-25 Outcome: recovered	Colitis ischaemic / epoetin zeta: unlikely related Gastrointestinal haemorrhage / epoetin zeta: unlikely related Mesenteric artery stenosis / epoetin zeta: unlikely related	Colitis ischaemic / epoetin zeta: unlikely related Gastrointestinal haemorrhage / epoetin zeta: unlikely related Mesenteric artery stenosis / epoetin zeta: unlikely related	Colitis ischaemic / epoetin zeta: not listed Gastrointestinal haemorrhage / epoetin zeta: not listed Mesenteric artery stenosis / epoetin zeta: not listed	Arteriosclerosis Coronary artery disease Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), batch: 1J245J1, subcutaneous, 10000 IU weekly since 2012-Feb-17 for renal anemia. On 2012-Jun-25 the patient developed high grade stenosis of arteria mesenterica superior with ischemic colitis and gastrointestinal hemorrhage. The event was treated with implant of vascular stent. The event resolved on 2012-Jul-05 and the patient was discharged the next day. Medical history included coronary heart disease, peripheral arterial occlusive disease and vascular sclerosis. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-054689 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-037-B012	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-02-07 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2012-09-05 Outcome: recovered Shunt thrombosis Onset: 2012-10-10 Outcome: recovered Venous stenosis Onset: 2012-10-10 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related Shunt thrombosis / epoetin zeta: unlikely related Venous stenosis / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable Shunt thrombosis / epoetin zeta: not assessable Venous stenosis / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed Shunt thrombosis / epoetin zeta: listed Venous stenosis / epoetin zeta: listed	Colon cancer Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), batch: 1N259C2, subcutaneous, 15000 IU weekly since 2012-Feb-17 for renal anemia. On 2012-Sep-05 the patient developed shunt occlusion. The patient was hospitalsed and a thrombectomy of basilica shunt and resection of the stenosis of left upper arm was performed. The event resolved on 2012-Sep-08 and the patient was discharged. Medical history included colon cancer since June 2012. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information was received the same day (2012-Dec-06): On 2012-Oct-10 the patient developed thrombosis and stenosis of vena brachiocephalica left and again formation of thrombus of basilica shunt. At the time of the event the patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), batch: 2E270F2, subcutaneous, 5000 IU weekly. The patient was hospitalised on 2012-Oct-12. A percutaneous transluminal angiography with ballon dilatation and endovascularprostethis was performed. The event resolved on 2012-Oct-13 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2012-Dec-17: Hospital letter received. No new information provided.
DE-STADA-106974 v1.0	Yes Other medical important condition	DE-039-B002	40 to 49	Female	amlodipine INN: amlodipine Start: not stated End: not stated Dosage: not stated Dosage text: not stated RoA: unknown SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-08-20 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angioedema Onset: 2015-11-10 Outcome: recovered	Angioedema / amlodipine: probable related Angioedema / epoetin zeta: possible related	Angioedema / amlodipine: probable related Angioedema / epoetin zeta: possible related	Angioedema / amlodipine: listed Angioedema / epoetin zeta: listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Nov-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2015-Aug-20 for renal anemia. After change of patient's hypertensive medication (amlodipine added) the patient developed Quincke's edema on 2015-Nov-10. Amlodipine was withdrawn and the event resolved on 2015-Nov-15. Medical history included hypertension. The reporter assessed the causal relationship between the event and SILAPO as possible. The reporter also stated the reaction as probable related to the calcium channel blocker.
DE-STADA-105623 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-039-B004	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-08-21 End: 2015-08-28 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2015-08-29 Outcome: not recovered	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: listed	Calcinosis Chronic kidney disease Hypertension Nephrogenic anaemia Obesity Peripheral arterial occlusive disease Sleep apnoea syndrome	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Aug-21 for renal anemia. On 2015-Aug-29 the patient developed bilateral pulmonary embolism and was hospitalised on 2015-Aug-30. The patient received anticoagulation therapy. The patient was discharged on 2015-Sep-21. The event was not yet resolved. In hospital the patient was changed to Aranesp (INN: darbepoetin) and after discharge the patient received Epoetin Hexal. A return to SILAPO administration was planned. Medical history included hypertension, obstructive sleep apnoea, calcinosis, peripheral arterial occlusive disease, obesity and dialysis dependent renal disease. The reporter assessed the causal relationship between the event and SILAPO as possible related.
DE-STADA-105625 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-039-B004	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-08-21 End: 2015-08-28 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2015-09-18 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Calcinosis Chronic kidney disease Hypertension Nephrogenic anaemia Obesity Peripheral arterial occlusive disease Pulmonary embolism Sleep apnoea syndrome	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Aug-21 for renal anemia. On 2015-Aug-29 the patient developed bilateral pulmonary embolism and was hospitalised on 2015-Aug-30 (cross ref.: DE-STADA-105623). During hospitalisation on 2015-Sep-18 the patient developed unstable angina pectoris. The patient underwent percuaneous transluminal coronary angioplasty and stent insertion. The event resolved and the patient was discharged on 2015-Sep-21. Medical history included hypertension, obstructive sleep apnoea, calcinosis, peripheral arterial occlusive disease, obesity and dialysis dependent renal disease. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-110504 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-039-B007	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-08-26 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac failure congestive Onset: 2015-10-07 Outcome: recovered	Cardiac failure congestive / epoetin zeta: unlikely related	Cardiac failure congestive / epoetin zeta: unlikely related	Cardiac failure congestive / epoetin zeta: not listed	Cardiomyopathy Diabetes mellitus Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jan-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Aug-26 for renal anemia. On 2015-Oct-07 the patient developed dyspnoea and pleural effusion. The patient was hospitalised on 2015-Oct-21 and congestive heart failure was diagnosed. The patient underwent thoracentesis and diuresis. The event resolved on 2015-Oct-28 and the patient was discharged. Medical history included diabetes mellitus, hypertension and cardiomyopathy. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-111410 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-039-B007	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-08-26 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac failure congestive Onset: 2015-11-23 Outcome: recovered	Cardiac failure congestive / epoetin zeta: unlikely related	Cardiac failure congestive / epoetin zeta: unlikely related	Cardiac failure congestive / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Feb-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Aug-26 for renal anemia. On 2015-Nov-23 the patient developed dyspnoea and weight gain. The patient was hospitalised on 2015-Nov-25 and congestive heart failure was diagnosed. The patient underwent diuresis. The event resolved on 2015-Dec-02 and the patient was discharged. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Cross ref.: DE-STADA-110504 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-041558 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-041-B007	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-08-09 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Acute myocardial infarction Onset: 2011-11-28 Outcome: recovered	Acute myocardial infarction / epoetin zeta: not related	Acute myocardial infarction / epoetin zeta: not assessable	Acute myocardial infarction / epoetin zeta: listed	Coronary artery disease Diabetes mellitus Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2011-Dec-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 1F221H1, SC 4000 IU weekly from 2011-Aug-09 for renal anemia. On 2011-Nov-28 the patient developed acute myocardial infarction during a hospital stay for shunt diagnostics. At the time of report the patient had not recovered. The treatment with SILAPO was interrupted. Patient's medical history included diabetes mellitus since 1997, hypertension, coronary heart disease since 1996 and peripheral arterial disease since November 1995. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2012-Jul-25: The event resolved on 2011-Dec-24. No further information was provided. The patient had a new myocardial infarction on 2012-Mar-02 (see case no.: DE-STADA-044636).
DE-STADA-044636 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-041-B007	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-08-09 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-03-02 Outcome: recovered Angina pectoris Onset: 2012-03-02 Outcome: not recovered	Angina pectoris / epoetin zeta: not related Myocardial infarction / epoetin zeta: not related	Angina pectoris / epoetin zeta: not assessable Myocardial infarction / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: not listed Myocardial infarction / epoetin zeta: listed	Coronary artery disease Diabetes mellitus Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Mar-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 1J242J1, SC 8000 IU weekly from 2011-Aug-09 for renal anemia. On 2012-Mar-02 he developed angina pectoris with troponin increase and myocardial infarction was diagnosed. The patient was hospitalised and received coronary angiography with stent placement. At the time of report the patient had not recovered. The treatment with SILAPO was interrupted. Patient's medical history included diabetes mellitus since 1997, hypertension, coronary heart disease since 1996 and peripheral arterial disease since November 1995. The reporter assessed the causal relationship between event and SILAPO as not related. Cross reference: DE-STADA-041558 (same patient). Follow-up information #1 was received on 2012-Jul-25: The myocardial infarction resolved on 2012-Mar-08. No further information was provided.
DE-STADA-072494 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-041-B007	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-08-09 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2014-02-01 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery bypass Coronary artery disease Diabetic nephropathy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2N333C3, SC 2000 IU weekly from 2011-Aug-09 for renal anemia. On 2014-Feb-01 the patient developed myocardial infarction while hospitalised for unspecified back pain. The patient died the same day due to myocardial infarction. Patient's medical history included diabetic nephropathy and preexisting coronary heart disease with 5 times coronary bypass. The reporter assessed the causal relationship between event and SILAPO as not related. Cross reference: DE-STADA-041558 and DE-STADA-044636 (same patient).
DE-STADA-052754 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-043-B001	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2011-09-19 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2012-09-21 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Anaemia Glomerulonephritis Hyperlipidaemia Hyperparathyroidism secondary Hypertension Intervertebral disc protrusion Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Oct-16. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously 2000 IE weekly since 2003-Sep-17 for renal anemia. On 2012-Sep-21 the patient developed shunt occlusion and was hospitalised. The event was treated and resolved on 2012-Sep-28. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2012-Dec-11: At the time of event the patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch 1M256C2, subcutaneously 2000 IE weekly since 2011-Sep-19. Medical history inlcuded glomerulonephritis, secondary hyperparathyroidism, hypertension, secondary anemia, lumbosacral disc protrusion and hyperlipidemia.
DE-STADA-068798 v1.0	Yes Involved persistence of significant disability or incapacity	DE-043-B004	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-04-05 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Aortic thrombosis Onset: 2013-07-02 Outcome: not recovered	Aortic thrombosis / epoetin zeta: not related	Aortic thrombosis / epoetin zeta: not assessable	Aortic thrombosis / epoetin zeta: listed	Cardiac failure Coronary artery disease Deep vein thrombosis Hydronephrosis Hypertension Hypothyroidism Insulin-requiring type 2 diabetes mellitus Ischaemic cardiomyopathy Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2M325C3, 9000 IU subcutaneously weekly since 2013-Apr-05 for renal anemia. On 2013-Jul-02 a CT examination revealed thrombosis of aorta descendes which was not resolved at the time of report. The patient was treated with acetylsalicylic acid and Plavix (INN: clopidogrel). The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history included peripheral arterial disease, hydronephrosis, coronary three-vessel disease, ischemic cardiomyopathy, chronic heart insufficiency, type 2 diabetes mellitus insulin-dependent, lower leg vein thrombosis, hypothyroidism and hypertension.
DE-STADA-072421 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-043-B004	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-04-05 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2014-01-02 Outcome: not recovered Skin necrosis Onset: 2014-01-02 Outcome: not recovered Wound Onset: 2014-01-02 Outcome: not recovered	Peripheral arterial occlusive disease / epoetin zeta: not related Skin necrosis / epoetin zeta: not related Wound / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable Skin necrosis / epoetin zeta: not related Wound / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not listed Skin necrosis / epoetin zeta: not listed Wound / epoetin zeta: not listed	Cardiac failure Coronary artery disease Deep vein thrombosis Hydronephrosis Hypertension Hypothyroidism Insulin-requiring type 2 diabetes mellitus Ischaemic cardiomyopathy Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2N336C3, 9000 IU subcutaneously weekly since 2013-Apr-05 for renal anemia. On 2014-Jan-02 the patient developed increased progressive peripheral arterial disease with necrosis of big toe and open wound on right heel. The patient was hospitalised the same day and discharged on 2014-Jan-15. The event was not resolved at the time of report. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history included peripheral arterial disease, hydronephrosis, coronary three-vessel disease, ischemic cardiomyopathy, chronic heart insufficiency, type 2 diabetes mellitus insulin-dependent, lower leg vein thrombosis, hypothyroidism, hypertension. Cross ref.: DE-STADA-068798 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-080465 v4.0	Yes Other medical important condition	DE-043-B008	80 to 89	Male	Ergenyl INN: valproic acid Start: 2012 End: not stated Dosage: 1 x 1300 mg per every 1 Day Dosage text: not stated RoA: unknown SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-06-08 End: 2014-05-26 Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2014-05-28 Outcome: not recovered Haemoglobin decreased Onset: not stated Outcome: not recovered	Drug ineffective / epoetin zeta: possible related Drug ineffective / valproic acid: not related Haemoglobin decreased / epoetin zeta: possible related Haemoglobin decreased / valproic acid: possible related	Drug ineffective / epoetin zeta: possible related Drug ineffective / valproic acid: not related Haemoglobin decreased / epoetin zeta: possible related Haemoglobin decreased / valproic acid: unknown	Drug ineffective / epoetin zeta: listed Drug ineffective / valproic acid: not applicable Haemoglobin decreased / epoetin zeta: listed Haemoglobin decreased / valproic acid: not applicable	Cerebral infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jul-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 3T01JV3, 15000 IU weekly, subcutaneously, since 2012-Jun-08 for renal anemia. On 2014-May-28 a lack of drug effect was noticed. The event was treated with Aranesp (INN: darbepoetin) but was not yet resolved. SILAPO was definitely discontinued (last administration of SILAPO on 2014-May-26). The reporter assessed the causal relationship between event and SILAPO as possible related. Medical history included brain infarction in October 2011 and obesity. Follow-up information #1 was received on 2014-Jul-15: After change to Aranesp the hemoglobin level did not normalise. It is not comprehensible why the hemoglobin level was decreased. Follow-up information #2 was received on 2014-Aug-19: On 2014-Aug-04 the hemoglobin level was slightly decreased to 5.82 mmol/l (0.2 mmol/l less than at last examination). On 2014-Aug-08 the dose of Aranesp was increased. Follow-up information #3 was received on 2014-Oct-01: At the time of report the hemoglobin level was slightly decreased to 5.76 mmol/l despite administration of Aranesp. At present the since 2012 administered drug Ergenyl (INN: valproic acid) was seen as the cause of hemoglobin decrease. Haemoccult tests were negative.
DE-STADA-129382 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-043-B009	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-05-01 End: not stated Dosage: 1 x 1500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2016-08-13 Outcome: recovered Angina unstable Onset: 2016-08-13 Outcome: recovered	Angina unstable / epoetin zeta: not related Transient ischaemic attack / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable Transient ischaemic attack / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed Transient ischaemic attack / epoetin zeta: listed	Acute kidney injury Anaemia Aortic valve stenosis Arterial catheterisation Atrial fibrillation Bacterial disease carrier Bronchitis Chronic kidney disease Coronary artery disease Dialysis Endocarditis Enteritis Factor XI deficiency Gouty arthritis Hypercalcaemia Hypertensive heart disease Hypertensive nephropathy Hypothyroidism Nephrogenic anaemia Osteoarthritis Pain Pneumonia aspiration Sepsis Spinal osteoarthritis Spondylolisthesis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Dec-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2013-May-01 for renal anemia. The current dose was 1500 IU weekly. The patient was hospitalised on 2016-Aug-13 due to unstable angina pectoris and transient ischaemic attack. The patient received aortic valve replacement and was discharged on 2016-Aug-20. The events had resolved on 2016-Aug-20 Last SILAPO administration prior onset was 2016-Aug-11. The SILAPO dose was not changed Medical history included aortic valve stenosis grade III, heterozygous hemophilia C, hypercalcaemia, acute obstructive bronchitis, acute enteritis due to clarithromycin, chronic renal insufficiency grade 5, dialysis since 2013-Mar after sepsis and hypertensive nephropathy, atrial catheter placement in 2013-Jun, acute renal failure in 2008, removal of arterial catheter after infection and shaldon catheter placement in 2013-Dec, condition after respiratory infection after E.coli respiration, rectal 3MRGN colonisation since 2013-Jul, hypertensive heart disease, multifactorial anaemia, coronary heart disease(in 2004 without relevant stenosis), permanent atrial fibrillation, condition after tricuspid valve endocarditis in 2009, hypothyroidism, chronic polyarthrosis, condition after gouty arthritis, spondyloarthrosis and pseudospondylolisthesis L4/L5 with chronic pain. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-073231 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-043-B011	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-09-19 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Finger amputation Onset: 2014-01-08 Outcome: not recovered Abscess Onset: not stated Outcome: not recovered	Abscess / epoetin zeta: unlikely related Finger amputation / epoetin zeta: unlikely related	Abscess / epoetin zeta: unlikely related Finger amputation / epoetin zeta: unlikely related	Abscess / epoetin zeta: not listed Finger amputation / epoetin zeta: not listed	Anaemia Cerebral artery embolism Cerebral infarction Coronary artery disease Hyperlipidaemia Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease Renal cyst	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 3000 IU subcutaneously weekly since 2011-Sep-19 for renal anemia. On 2014-Jan-08 the patient was hospitalised for amputation of left forefinger after an abscess. The event was not resolved at the time of report. Medical history included kidney cysts, coronary heart disease, hyperlipidemia, hypertension, cerebral embolism, secondary hyperparathyroidism, secondary anemia, peripheral arterial occlusive disease and subacute brain infarction. The reporter assessed the causal relationship between the event and SILAPO as unlikely related.
DE-STADA-049974 v2.0	Yes Patient died	DE-043-B013	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-09-19 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2012-07-01 Outcome: fatal	Pulmonary embolism / epoetin zeta: not related	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Anaemia Arrhythmia Cardiac failure Glomerulonephritis Hyperparathyroidism Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 6000 IU weekly since 2011-Sep-19 for renal anemia. On 2012-Jul-01 the patient died due to pulmonary embolism. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2012-Dec-11: On 2012-Jul-01 the patient suddenly died at home. The suspicion of pulmonary embolism was made. The cause of death could not be clearly defined. At the time of event the patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 1M250N1, SC 8000 IU weekly. Medical history included glomerulonephritis, arrhythmia, hypertension, secondary anemia, renal hyperparathyroidism and cardiac insufficiency.
DE-STADA-154621 v1.0	Yes Involved persistence of significant disability or incapacity	DE-045-B002	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-25 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2016-11-15 Outcome: not recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Dec-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Aug-25 for renal anemia. The current dose was 9000 IU weekly and batch 6S031U6. On 2016-Nov-15 the patient developed peripheral arterial occlusive disease. The event was treated by walking training but was still present. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-104577 v2.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-045-B003	40 to 49	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2011-11-22 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2015-04-01 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Hyperparathyroidism secondary Hypertension Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously, 9000 IU weekly since 2011-Nov-22 for renal anemia. On 2015-Apr-01 the patient developed peripheral arterial occlusive disease grade IIB. The patient was hospitalised and percutaneous transluminal angioplasty was performed. The patient was discharged on 2015-Apr-04. The event had not resolved. The dose of SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2015-Oct-12: Hospital letter received. The patient was discharged on 2015-Apr-04 in good general condition. Medical history included dialysis requiring renal insufficiency, secondary hyperparathyroidism, hypertension and insulin dependent diabetes mellitus. Additional information was received on 2015-Oct-19: The administered batch of SILAPO was 4V069V4.
DE-STADA-104590 v2.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-045-B003	40 to 49	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2011-11-22 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Coronary artery occlusion Onset: 2015-05-07 Outcome: not recovered Arterial occlusive disease Onset: 2015-05-07 Outcome: not recovered Coronary artery disease Onset: 2015-05-07 Outcome: not recovered Peripheral artery stenosis Onset: 2015-05-07 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: unlikely related Coronary artery disease / epoetin zeta: unlikely related Coronary artery occlusion / epoetin zeta: unlikely related Peripheral artery stenosis / epoetin zeta: unlikely related	Arterial occlusive disease / epoetin zeta: not assessable Coronary artery disease / epoetin zeta: not assessable Coronary artery occlusion / epoetin zeta: not assessable Peripheral artery stenosis / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not listed Coronary artery disease / epoetin zeta: not listed Coronary artery occlusion / epoetin zeta: not listed Peripheral artery stenosis / epoetin zeta: not listed	Chronic kidney disease Hyperparathyroidism secondary Hypertension Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously, 9000 IU weekly since 2011-Nov-22 for renal anemia. The patient was hospitalised on 2015-May-06. On 2015-May-07 coronary heart disease with occlusion of arteria coronaria dextra and arterial occlusive disease with stenosis of arteria iliaca communis right and arteria iliaca interna left was diagnosed. The patient was discharged on 2015-May-07 without intervention. The event was not resolved. The dose of SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-104577 (same patient) Follow-up information #1 was received on 2015-Oct-12: Hospital letter received. The patient was hospitalised on 2015-May-06 for coronary angiography and iliofemoral angiography which revealed the described events. Medical history incuded chronic renal insufficiency, secondary hyperparathyroidism, hypertension, peripheral arterial occlusive disease grade IIB and insulin dependent diabetes mellitus. Additional information was received on 2015-Oct-19: The administered batch of SILAPO was 4V069V4.
DE-STADA-069620 v2.0	No	DE-045-B009	50 to 59	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2013-08-09 End: 2013-10-04 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Hypertrichosis Onset: 2013-09 Outcome: recovered	Hypertrichosis / epoetin zeta: possible related	Hypertrichosis / epoetin zeta: possible related	Hypertrichosis / epoetin zeta: not listed	Migraine Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Dec-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 92499261202, 3000 I.E. weekly subcutaneously since 2013-Aug-09 for renal anemia. On 2013-Sep-01 the patient complained increased hair growths (hypertrichosis). SILAPO therapy was discontinued on 2013-Oct-04. The event resolved on 2013-Nov-01. Medical history included migraine since May 2010. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up information #1 was received on 2013-Dec-10: The increase of hair growth started in September 2013 and was resolved on 2013-Nov-15.
DE-STADA-082827 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-045-B010	60 to 69	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2012-04-04 End: 2013-06-28 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial stenosis Onset: 2014-05-08 Outcome: recovered Venous stenosis Onset: 2014-05-08 Outcome: recovered	Arterial stenosis / epoetin zeta: not related Venous stenosis / epoetin zeta: not related	Arterial stenosis / epoetin zeta: not assessable Venous stenosis / epoetin zeta: not assessable	Arterial stenosis / epoetin zeta: not listed Venous stenosis / epoetin zeta: not listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Aug-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2012-Apr-04 for renal anemia. On 2014-May-08 the patient developed arterial stenosis of forearm and venous stenosis on upper left shunt arm. The patient was hospitalised and underwent percutaneous transluminal angioplasty of shunt stenosis. The event resolved and the patient was discharged on 2014-May-09. The last SILAPO batch used before the reaction onset was 2J318K2. The SILAPO administration was paused since 2014-Jul-01 due to persisting hemoglobin value of 11 g/dl without Erythropoiesis-Stimulating Agent. Medical history included obesity. The reporter assessed the causal relationship between the event and SILAPO as not related. Follow-up information #1 was received on 2014-Dec-29: SILAPO therapy was discontinued on 2014-Aug-18. Follow-up information #2 was received on 2015-Oct-06: The dose of SILAPO was changed to 3000 IU weekly and therapy end and last dose of SILAPO was corrected to 2013-Jun-28.
DE-STADA-089427 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-045-B011	70 to 79	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2012-02-07 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2014-11-27 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Diverticulitis Hyperlipidaemia Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Obesity Renal failure chronic Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Dec-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously since 2012-Feb-07 for renal anemia. The administered batch at the time of report was 4T042U4. On 2014-Nov-27 the patient developed dialysis shunt occlusion of Cimino fistula. Therapy for the event was thrombectomy and patchplasty of Cimino fistula. The event resolved the same day and the patient was discharged on 2014-Nov-28. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included chronic renal insufficiency, sec. hyperparathyroidism, hypertension, diabetes mellitus type 2, adipositas, hyperlipidemia and sigmoid verticulosis.
DE-STADA-154608 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-045-B012	70 to 79	Male	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2017-05-31 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2017-11-17 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Acute myocardial infarction Bladder neoplasm Cataract Chronic kidney disease Gastrointestinal angiodysplasia Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Prostate cancer Renal artery stenosis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Dec-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-May-31 for renal anemia. The current dose was 4000 IU weekly. On 2017-Nov-17 the patient developed ischaemic stroke and was hospitalised. The patient received mechanical thrombectomy and the event resolved with sequel on 2017-Nov-19. The patient was discharged on 2017-Dec-12. The SILAPO treatment was continued. The reporter assessed the causal relationship between event and SILAPO as not assessable. Medical history included chronic renal insufficiency, secondary hyperparathyroidism, hypertension, Non-ST-Elevated Myocardial Infarction, angiodysplasia bulbitis duodeni, renal artery stenosis, bladder tumor, prostatic cancer, cataract.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-135485 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-045-B013	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-08-23 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt stenosis Onset: 2016-12-02 Outcome: recovered	Shunt stenosis / epoetin zeta: unlikely related	Shunt stenosis / epoetin zeta: not assessable	Shunt stenosis / epoetin zeta: listed	Atrial septal defect Chronic kidney disease Congenital cystic kidney disease Foot fracture Hyperparathyroidism secondary Hypertension Hysterectomy Malignant melanoma Nephrogenic anaemia Urinary tract infection	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Aug-23 for renal anemia. The current dose of SILAPO was 9000 IU weekly and batch: 92530621302. On 2016-Dec-02 the patient was hospitalised due to stenosis and consecutive flow disorder of dialysis fistula (Cimino shunt). On 2017-Dec-03 a percutaneous transluminal angiography was performed and the event resolved the same day. The therapy with SILAPO was continued. Medical history included chronic renal insufficiency, autosomal dominant polycystic kidney disease, secondary renal hyperparathyroidism and recurrent urinary tract infection, hypertension, atrial septal defect, malignant melanoma of left foot in 2005, hysterectomy in 2000 and fracture of os metatarsal in November 2016. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2017-Dec-20: The event resolved on 2016-Dec-02 and the patient was discharged the same day. The administered batch of SILAPO was 65031U6.
DE-STADA-143181 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-045-B013	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-08-23 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2017-05-27 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Chronic kidney disease Congenital cystic kidney disease Hyperparathyroidism secondary Nephrogenic anaemia Urinary tract infection Venous stenosis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jul-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Aug-23 for renal anemia. The current dose of SILAPO was 3000 IU weekly and batch: 92530621302. On 2017-May-26 the patient developed acute shunt occlusion of left arm and was hospitalised. On 2017-May-27 a percutaneous angiography was performed and the event resolved the same day. The therapy with SILAPO was continued. Medical history included chronic renal insufficiency, autosomal dominant polycystic kidney disease, secondary renal hyperparathyroidism and recurrent urinary tract infection. In December 2012 a cimino shunt in left arm was inserted. In December 2016 a percutaneous angiography of a venous stenosis was performed. Cross ref.: DE-STADA-135485 (same patient). The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2017-Sep-23: The event onset date was corrected to 2017-May-27 Follow-up information #2 was received on 2017-Dec-20: The patient underwent percutaneous angioplasty and the event resolved. The last administration of SILAPO prior to the event was 2017-May-24 and the administered batch was 5U064W5.
DE-STADA-057737 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-045-B015	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-08-30 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2013-01-31 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Hip dysplasia Hypercholesterolaemia Hypertension Nephrogenic anaemia Obesity Peripheral arterial occlusive disease Pneumonia Renal failure chronic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Feb-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 2E262F2, 12000 I.E. weekly intravenous since 2011-Aug-30 for renal anemia. On 2013-Jan-31 the patient was hospitalised with myocardial infarction. The patient received conservative treatment and the event resolved with sequelae on 2013-Feb-07. The patient was discharged on 2013-Feb-07. The treatment with SILAPO was intercepted. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history inlcuded coronary threevessel disease since 1998. Follow-up information #1 was received on 2013-Apr-05: The patient's birthdate was provided. Patient's medical history included adipositas, hypertension, hypercholesterolemia, nosocomial pneumonia, chronic renal insufficiency, peripheral arterial disease and chronic hip dysplasia. Cross ref.: DE-STADA-059115 (same patient).
DE-STADA-059115 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-045-B015	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2011-08-30 End: 2013-03-16 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2013-03-18 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Apr-02 and on 2013-Apr-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 2E262F2, 12000 I.E. weekly intravenous since 2011-Aug-30 for renal anemia. On 2013-Mar-18 the patient was hospitalised with myocardial infarction described as angina pectoris requiring reanimation. The patient was resuscitated but died on 2013-Mar-21. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history inlcuded coronary threevessel disease, hypertension and peripheral arterial occlusive disease all since 1998. Cross ref.: DE-STADA-057737 (same patient)
DE-STADA-149191 v1.0	Yes Other medical important condition	DE-045-B016	30 to 39	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-25 End: 2016-11-14 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2016-11-14 Outcome: recovered	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed	Hypertension Infectious pleural effusion Lymphadenopathy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-25 and on 2017-Sep-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2016-Aug-25 for renal anemia. The current dose of SILAPO was 12000 IU subcutaneously weekly. The last administered batch was 6T041U6. The last administration of SILAPO was 2016-Nov-14. On 2016-Nov-18 the patient was discharged from study due to missing haemoglobin increase (lack of drug effect). The haemoglobin value was 8.1 g/dl at study start and 8.9 g/dl at drop out. The patient changed to another erythropoiesis stimulating product (Aranesp - darbepoetin alfa). After change the haemoglobin increased as: 9.6 g/dl on 2016-Dec-06 9.7 g/dl on 2016-Dec-12 10.2 g/dl on 2016-Dec-26 and at the time of report 13.3 g/dl Medical history included hypertension, lymphadenopathy and pleural empyema since May 2016. The reporter assessed the causal relationship between event and SILAPO as possible related. It was also reported that the patient tends to have fluctuating Hb values, but is currently stable.
DE-STADA-076004 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-047-B002	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-03-15 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2014-03-24 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Apr-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) batch: 3E357G3/08-2015, 6000 IU weekly intravenously since 2012-Mar-15 for renal anaemia. On 2014-Mar-24 the patient developed myocardial infarction. The patient was hospitalised on 2014-Mar-24 and received conservative treatment. The event recovered on 2014-Apr-03 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as unlikely related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druas only)	Company causality (Susoect druas only)	Listedness (Susoect druas only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-055188 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-048-B008	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-07-03 End: 2012-12-04 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-12-04 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Aortic valve replacement Benign prostatic hyperplasia Coronary artery disease Dysphagia Hypertension Hyperuricaemia Mitral valve disease Nephrogenic anaemia Non-Hodgkin's lymphoma Pulmonary hypertension Renal failure chronic	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Dec-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) from 2012-Jul-03 to 2012-Nov-01 for renal anemia. The patient was hospitalised on 2012-Dec-04 with subacute myocardial infarction. His condition deteriorated and the patient died on 2012-Dec-10. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history inlcuded chronic renal insufficiency, coronary heart disease, aortic valve replacement, mitral valve insufficiency, hypertension (arterial and pulmonary), malignant Non-Hodgkin's lymphoma, hyperuricemia, dysphagia and prostatic hyperplasia. Follow-up information #1 was received on 2013-Feb-07: The patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously from 2012-Jul-03 to 2012-Dec-04 for renal anemia. The reporter assessed the causal relationship between the event myocardial infarction and SILAPO as unlikely related.
DE-STADA-066356 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-048-B008	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-01-06 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2013-08-13 Outcome: fatal	Cerebral haemorrhage / epoetin zeta: not related	Cerebral haemorrhage / epoetin zeta: not assessable	Cerebral haemorrhage / epoetin zeta: listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-26 and 2013-Sep-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 4000 IU weekly since 2012-Jan-06 for renal anemia. On 2013-Aug-13 the patient developed speech disorder and hemiparesis left arm and a cerebral haemorrhage was detected. The patient died on 2013-Aug-30. Medical history included hypertension. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-071932 v3.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-048-B011	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-06-22 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Venous occlusion Onset: 2014-01-03 Outcome: fatal	Venous occlusion / epoetin zeta: not assessable	Venous occlusion / epoetin zeta: not assessable	Venous occlusion / epoetin zeta: listed	Cerebrovascular accident Hyperkalaemia Hypertension Metabolic acidosis Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure Renal transplant	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jan-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2M324C3, 6000 IU subcutaneously weekly since 2012-Jun-22 for renal anemia. On 2014-Jan-01 the patient was hospitalised with venous occlusion of arteria brachialis left. The patient received bypass surgery. The patient's general condition worsened and he died due to multi organ failure on 2014-Jan-05. The reporter assessed the causal relationship between the event and SILAPO as not assessable. Patient's medical history included apoplexy in 1997 and 2002, renal insufficiency, hyperkalemia, metabolic acidosis, renal transplant in 12/1998, hypertension and peripheral occlusive disease. Follow-up information #1 was received on 2014-Feb-19: The reaction onset date was corrected to 2014-Jan-03. Follow-up information #2 was received on 2014-Mar-04: The hospitalisation date was corrected to 2014-Jan-03.
DE-STADA-049759 v4.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-048-B017	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2011-11-25 End: 2014-08-21 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2012-05-07 Outcome: recovered Myocardial infarction Onset: 2014-09-23 Outcome: fatal	Myocardial infarction / epoetin zeta: not related Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Myocardial infarction Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2012-Jul-19. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 8000 IU weekly since 2011-Nov-25 for renal anemia. On 2012-May-07 the patient developed myocardial infarction and was hospitalised. The patient received revascularisation and was discharged on 2012-May-23. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2014-Oct-01: The patient died on 2014-Sep-23 probably due to myocardial infarction. There was no causal relationship to SILAPO. Follow-up information #2 was received on 2014-Oct-06: On 2014-Sep-23 the patient developed myocardial infarction and died. SILAPO was paused since 2014-Aug-21. The reporter assessed the causal relationship between event and SILAPO as not assessable. Medical history included coronary heart disease and reinfarction. Follow-up information #3 was received on 2014-Oct-10: The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-067818 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-048-B023	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-01-03 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial occlusive disease Onset: 2013-05-13 Outcome: not recovered	Arterial occlusive disease / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2J322K2, 8000 IU subcutaneously weekly since 2012-Jan-03 for renal anemia. On 2013-May-13 the patient developed occlusion of artery tibialis posterior left. The patient was hospitalised and discharged on 2013-May-17. The event was not resolved at the time of report. Medical history included peripheral arterial disease. The reporter assessed the causal relationship as not related to Silapo.
DE-STADA-060437 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-049-B005	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-01-14 End: not stated Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2013-04-18 Outcome: not recovered	Pulmonary embolism / epoetin zeta: unlikely related	Pulmonary embolism / epoetin zeta: possible related	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-May-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC since 2013-Jan-14 for renal anemia. On 2013-Apr-18 the patient developed exertional dyspnoea. In the lung scintigram a pulmonary embolism was suspected which was not resolved at the time of report. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-108461 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-049-B005	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-01-14 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2014-05-02 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Bile duct stone Cholelithiasis Diabetes mellitus Hyperlipidaemia Hyperparathyroidism secondary Hypertension Hypervolaemia Nephrogenic anaemia Peripheral arterial occlusive disease Prostate cancer Renal failure Urinary retention	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Dec-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) (batch: 2N334C3), SC since 2013-Jan-14 for renal anemia. The patient was hospitalised due to peripheral arterial disease on 2014-Apr-28, at the hospital the patient developed a mild myocardial infarction (NSTEMI) on 2014-May-02. The outcome was reported to be recovered the same day. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2015-Dec-18: The patient was hospitalised for a scheduled amputation of toe on 2014-Apr-28. During dialysis the patient developed myocardial infarction on 2014-May-02. The event was treated interventional. The patient was discharged in good general condition on 2014-May-06. Medical history included renal insufficiency, secondary hyperparathyroidism, hypertension, diabetes mellitus, hyperlipidemia, pulmonary hypervolaemia, prostatic adenocarcinoma, overflow bladder, obstructive choledocholithiasis and cholecystolithiasis.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-057958 v3.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-050-B002	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2012-03-19 End: 2012-12-20 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2012-12-16 Outcome: fatal	Cerebral haemorrhage / epoetin zeta: not related	Cerebral haemorrhage / epoetin zeta: not assessable	Cerebral haemorrhage / epoetin zeta: listed	Aortic aneurysm Aortic bypass Arthritis Cholecystectomy Femoral artery aneurysm Nephrogenic anaemia Polyarthritis Renal hypertension Vascular graft	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Mar-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 3000 IU weekly since 2012-Mar-19 for renal anemia. The patient was hospitalised with cerebral haemorrhage on 2013-Feb-06. The patient died. Medical history included condition after endovascular prosthesis in December 2011, aortic aneurysm in 1995, aortic prosthesis in 1995, aneurysm of A. femoralis in 1998, chronic polyarthritis since 1998, cholecystectomy in March 2010, polypectomia of colon in March 2010, renal hypertension since January 2005 and oligoarthritis. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2013-Mar-13: The patient was hospitalised with cerebral haemorrhage on 2012-Dec-20 and not on 2013-Feb-06 as previously reported. The patient died on 2013-Feb-06. Follow-up information #2 was received on 2013-Apr-04: The start of event and hospitalisation was corrected to 2012-Dec-16.
DE-STADA-056779 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-052-B001	70 to 79	Female	SILAPO INN: epoetin zeta Start: 2012-07-27 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt thrombosis Onset: 2013-01-02 Outcome: recovered	Shunt thrombosis / epoetin zeta: not related	Shunt thrombosis / epoetin zeta: not assessable	Shunt thrombosis / epoetin zeta: listed	Chronic obstructive pulmonary disease Coronary artery disease Hypertension Obesity Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Feb-05 and 2013-Feb-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), batch: 2E269F2, subcutaneous, 8000 IU weekly since 2012-Jul-27 for renal anemia. On 2013-Jan-02 a dysfunction of the long-term central venous catheter (Permcath) was noticed. The patietn was hospitalised and the event was treated by lysis with urokinase. Therapy with SILAPO was interrupted. The event resolved on 2013-Jan-03 and the patient was discharged. Medical history included diabetes mellitus type 2, hypertension, coronary heart disease, COPD and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-105316 v2.0	Yes Patient died	DE-052-B002	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2014-05-10 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-07-04 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) SC 4000 IU weekly since 2013-May-10 for renal anemia. On 2015-Jul-04 the patient suddenly died at home due to myocardial infarction. The last administration of SILAPO was on 2015-Jul-03. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2016-Oct-06: The patient's medical history included also obesity.
DE-STADA-065524 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-052-B007	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2012-07-17 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2013-07-30 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Carotid artery stenosis Coronary artery disease Endarterectomy Hypertension Monoclonal gammopathy Nephrogenic anaemia Peripheral arterial occlusive disease Tobacco abuse Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Sep-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) batch: 2N330C3/05-2015, SC 8000 IU weekly since 2012-Jul-17 for renal anemia. On 2013-Jul-30 the patient developed myocardial infarction with subtotal closed vein bypass (triggered by preexisting acute pancreatitis) and was hospitalised. The event resolved and the patient was discharged on 2013-Aug-04. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included three vessel disease, diabetes mellitus type 2, hypertension, peripheral artery occlusive disease, carotid stenosis and condition after thrombo-endarterectomy, monoclonal gammopathy and chronic tobacco abuse.
DE-STADA-148495 v2.0	Yes Patient died	DE-054-B024	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2017-02-17 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac arrest Onset: 2017-06-16 Outcome: fatal	Cardiac arrest / epoetin zeta: not related	Cardiac arrest / epoetin zeta: not assessable	Cardiac arrest / epoetin zeta: not listed	Coronary artery disease Hyperlipidaemia Hypertension Myocardial infarction Nephrogenic anaemia Renal failure Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Feb-17 for renal anemia. The current SILAPO dose was 3000 IU weekly. On 2017-Jun-16 the patient died due to myocardial infarction. Medical history included renal insufficiency, coronary heart disease, myocardial infarction, hyperlipidemia, hypertension and type 2 diabetes mellitus. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2017-Sep-27: The reporter corrected the cause of death to cardiac arrest, no adverse reaction / event of special interest.
DE-STADA-126828 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-055-B001	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-11-16 End: 2016-10-21 Dosage: 1 x18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2016-10-17 Outcome: fatal	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Glomerulonephritis membranous Ileus Laparotomy Nephrogenic anaemia Transurethral prostatectomy	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Nov-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 18000 IU weekly subcutaneously since 2015-Nov-16 for renal anemia. On 2016-Oct-17 peripheral arterial occlusive disease stage IV was diagnosed, and on 2016-Oct-25 the patient was hospitalised. Percutaneous transluminal angioplasty with stent insertion was performed. The patient died on 2016-Oct-27. Patient's medical history included laparotomy due to obstructive ileus, transurethral resection prostate and membranous glomerulonephritis. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Follow-up information #1 was received on 2020-May-26: The batch number of the administered product was 6Q024R6.
DE-STADA-072492 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-055-B004	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-11-25 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac disorder Onset: 2014-01-17 Outcome: fatal Lower limb fracture Onset: 2014-01-14 Outcome: unknown	Cardiac disorder / epoetin zeta: not related Lower limb fracture / epoetin zeta: not related	Cardiac disorder / epoetin zeta: not assessable Lower limb fracture / epoetin zeta: not related	Cardiac disorder / epoetin zeta: listed Lower limb fracture / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Feb-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU subcutaneously weekly since 2013-Nov-25 for renal anemia. On 2014-Jan-14 the patient was hospitalised for thigh neck fracture after a fall. On the third day of hospitalisation the patient died possible due to cardiac event. The reporter assessed the causal relationship between the event and SILAPO as not related. An autopsy was not performed. Follow-up information #1 was received on 2014-Jun-05: The administered batch no of SILAPO was 2N335C3/05-2015.
DE-STADA-156846 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-055-B010	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2017-11-06 End: 2017-12-11 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2017-12-13 Outcome: fatal Gangrene Onset: 2017-12-13 Outcome: fatal	Gangrene / epoetin zeta: possible related Peripheral arterial occlusive disease / epoetin zeta: possible related	Gangrene / epoetin zeta: possible related Peripheral arterial occlusive disease / epoetin zeta: possible related	Gangrene / epoetin zeta: not listed Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Feb-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously for renal anemia since 2017-Nov-06. The current dose was 4000 IU weekly. The current batch was 7002407. On 2017-Dec-13 experienced progression of peripheral arterial occlusive disease and gangrene of toes and was hospitalised. The patient died on 2018-Jan-08 due to progression of peripheral arterial occlusive disease and sepsis. The last SILAPO administration was on 2017-Dec-11. The reporter assessed the causal relationship between the events and SILAPO as possible related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-151858 v1.0	Yes Other medical important condition	DE-055-B028	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-16 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	Marcumar INN: phenprocoumon Indication: Anticoagulant therapy	Shunt occlusion Onset: 2017-08-14 Outcome: recovered	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: listed	Factor II mutation Factor V Leiden mutation Hypercoagulation Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-03 and on 2017-Nov-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Nov-16 for renal anemia. The current dose of SILAPO was 2000 IU weekly. Batch number was 60054W6. On 2017-Aug-14 the patient developed shunt occlusion. A percutaneous angiography was performed and the event resolved on 2017-Aug-16. The therapy with SILAPO was continued. Medical history included obesity and thrombophilia diagnosed 2000 (Prothrombin mutation and Factor V Leiden heterozygote). The patient received an oral anticoagulation therapy with Marcumar (INN: phenprocoumon). The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-068643 v2.0	Yes Other medical important condition	DE-055-B036	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-04-08 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2013-09-23 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Foot amputation Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2013-Nov-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 12000 IU weekly subcutaneously since 2013-Apr-08 for renal anemia. On 2013-Sep-23 the patient developed dialysis shunt occlusion. The event was treated with lysis and shunt transluminal angioplasty and resolved the same day. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included peripheral arterial disease since 1999 with several surgeries and finally partly foot amputation. Follow-up information #1 was received on 2014-Jun-05: The administered batch no of SILAPO was 2J3012.
DE-STADA-182336 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-055-B038	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-10-31 End: not stated Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Coronary artery disease Onset: 2019-03-07 Outcome: recovered Coronary artery stenosis Onset: 2019-03-07 Outcome: recovered	Coronary artery disease / epoetin zeta: unlikely related Coronary artery stenosis / epoetin zeta: unlikely related	Coronary artery disease / epoetin zeta: not assessable Coronary artery stenosis / epoetin zeta: not assessable	Coronary artery disease / epoetin zeta: not listed Coronary artery stenosis / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jun-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Oct-31 for renal anemia. The last dose of SILAPO was administered on 2018-Sep-03. Since that no SILAPO administration was necessary. Batch number was not provided. On 2019-Mar-07 the patient developed double vessel disease with ramus circumflexus stenosis. The patient was hospitalised. A percutaneous transluminal coronary angioplasty was performed and drug eluting stent was implemented. The event resolved and the patient was discharged on 2019-Mar-08. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2019-Jun-18. The hospital letter was received. No new relevant information reported.
DE-STADA-191856 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-055-B038	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-10-31 End: not stated Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Coronary artery occlusion Onset: 2019-08-06 Outcome: recovered	Coronary artery occlusion / epoetin zeta: unlikely related	Coronary artery occlusion / epoetin zeta: not assessable	Coronary artery occlusion / epoetin zeta: not listed	Congenital cystic kidney disease Dementia Alzheimer's type Gout Hyperlipidaemia Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Dec-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Oct-31 for renal anemia. The last dose of SILAPO was administered on 2019-Jun-10. Batch number BW03BK8. On 2019-Aug-06 the patient developed pathological stress echocardiogram. Therefore percutaneous coronary intervention of the coronary occlusion of right coronary artery with percutaneous transluminal coronary angioplasty and stents were performed. The event resolved on 2019-Aug-07 and the patient was discharged on 2019-Aug-08. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included autosomal dominant polycystic kidney disease, arterial hypertension, hyperlipoproteinemia, peripheral arterial occlusive disease, beginning Alzheimer disease, gout. Cross ref.: DE-STADA-182336 (same patient).
DE-STADA-153463 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-055-B039	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-16 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral artery occlusion Onset: 2017-06-19 Outcome: not recovered Coronary artery disease Onset: 2017-10-09 Outcome: recovered Peripheral artery stenosis Onset: 2017-06-19 Outcome: not recovered	Coronary artery disease / epoetin zeta: unlikely related Peripheral artery occlusion / epoetin zeta: unlikely related Peripheral artery stenosis / epoetin zeta: unlikely related	Coronary artery disease / epoetin zeta: not assessable Peripheral artery occlusion / epoetin zeta: not assessable Peripheral artery stenosis / epoetin zeta: not assessable	Coronary artery disease / epoetin zeta: not listed Peripheral artery occlusion / epoetin zeta: not listed Peripheral artery stenosis / epoetin zeta: not listed	Chronic kidney disease Diverticulitis Gout Haemodialysis Hyperuricaemia Nephrogenic anaemia Transient ischaemic attack	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Nov-16 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was not provided. On 2017-Jun-19 the patient developed occlusion of superficial femoral artery left and stenosis of superficial femoral artery right. The patient was hospitalised from 2017-Jun-26 to 2017-Jun-28. The event was not yet resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2018-Feb-03 and on 2018-Feb-05: On 2017-Oct-09 the patient was hospitalised due to progression of known coronary 3 vessel disease. Therapy was coronary angiography with successful recanalisation of RCA stenosis. The therapy with SILAPO was continued. The current batch was 6X084X6. Medical history included thromboendarterectomy after transient ischemic attack in 2008, chronic renal insufficiency, start of hemodialys on 2015-Jul-13, sigmoid resection in 2007 at diverticulitis, hyperuricaemia and recurrent gout attack. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-164581 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-055-B039	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-16 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	Calciumacetat-Nefro 500 mg INN: calcium acetate Indication: Product used for unknown indication carvedilol INN: carvedilol Indication: Product used for unknown indication clopidogrel INN: clopidogrel Indication: Product used for unknown indication Fosrenol 1000 INN: lanthanum carbonate Indication: Product used for unknown indication ramipril INN: ramipril Indication: Product used for unknown indication simvastatin INN: simvastatin Indication: Product used for unknown indication	Peripheral artery restenosis Onset: 2018-03-05 Outcome: recovered	Peripheral artery restenosis / epoetin zeta: unlikely related	Peripheral artery restenosis / epoetin zeta: not assessable	Peripheral artery restenosis / epoetin zeta: not listed	Coronary artery disease Diverticulitis Hypertension Hyperuricaemia Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jun-13 and on 2018-Jun-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Nov-16 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was 70030Q7. On 2018-Mar-05 the patient developed restenosis of superficial femoral artery right and was hospitalised. A percutaneous transluminal angioplasty with stent insertion was performed. The patient was hospitalised from 2018-Mar-05 to 2018-Mar-07. The event resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included peripheral occlusive disease, hypertension, renal insufficiency, coronary 2 vessel disease, sigmoid resection in January 2007 at diverticulitis, hyperuricaemia. Concomitant medication was clopidogrel, simvastatin, Calciumacetat-Nefro 500 mg (INN: calcium acetate), Fosrenol 1000 (INN: lanthan), carvedilol and ramipril. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-153463 (same patient).
DE-STADA-096398 v2.0	Yes Other medical important condition	DE-057-B003	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2013-12-17 End: not stated Dosage: not stated Dosage text: not stated RoA: unknown	N/A	Drug ineffective Onset: not stated Outcome: unknown	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: not assessable	Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Apr-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2013-Dec-17 for renal anemia. On an unknown date the lack of drug effect was noted. No further information was provided. Follow-up #1 was received on 2015-May-11: The study nurse reported that this report can be deleted as it was created erroneously. Therefore this case was nullified.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-079913 v5.0	Yes Involved or prolonged inpatient hospitalisation	DE-057-B007	70 to 79	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2013-12-19 End: not stated Dosage: 2 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Anaemia Onset: 2014-06-15 Outcome: recovered Syncope Onset: 2014-06-15 Outcome: recovered	Anaemia / epoetin zeta: unlikely related Syncope / epoetin zeta: unlikely related	Anaemia / epoetin zeta: possible related Syncope / epoetin zeta: unlikely related	Anaemia / epoetin zeta: listed Syncope / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Jun-03 and on 2014-Jun-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2013-Dec-19 for renal anemia. On 2014-Jun-15 the patient developed syncope due to anemia. The patient was hospitalised and received erythrocytes. The event resolved on 2014-Jun-19 and the patient was discharged on 2014-Jun-25. The dose of SILAPO was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2014-Jul-01: The patient's hemoglobin level was 5.7 g/dl on 2014-May-28. After administration of erythrocytes concentrates the hemoglobin level was 6.8 g/dl on 2014-Jul-01. Follow-up information #2 was received on 2014-Jul-18: The patient's hemoglobin level was 5.8 g/dl on 2014-Jul-15. Follow-up information #3 was received on 2014-Jul-24: The underlying disease was suspected as cause for the low hemoglobin level. The SILAPO dose was increased from 4000 IU twice weekly to 5000 IU twice weekly. Next regular due date for Hb tests will be 2013-Aug-05. Follow-up information #4 was received on 2014-Aug-20, on 2014-Aug-28 and on 2014-Aug-29: At examination on 2014-Aug-12 the hemoglobin level was 5.2 mmol/l despite increase of SILAPO. SILAPO was increased to 6000 IU twice weekly. The previously entered unit for hemoglobin levels was corrected from g/dl to mmol/l.
DE-STADA-083944 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-062-B002	unknown	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2013-12-10 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebrovascular accident Onset: 2014-06-20 Outcome: unknown	Cerebrovascular accident / epoetin zeta: unlikely related	Cerebrovascular accident / epoetin zeta: not assessable	Cerebrovascular accident / epoetin zeta: listed	Cerebrovascular insufficiency Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2014-Sep-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia. A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2013-Dec-10 for renal anemia. On 2014-Jun-20 the patient suffered from stroke described as reapoplex under multi infarction syndrome in hypertensive encephalopathy which lasted for two days. The patient was hospitalised on 2014-Jun-20 due to the event. She was treated conservatively and dialysis was initiated. The dosage of the suspected drug was increased, The patient was discharged on 2014-Sep-01, Patient's medical history was reported as cerebrovascular damage. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-117807 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-063-B003	50 to 59	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-11-21 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-04-07 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-May-30 and on 2016-May-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 9000 IU weekly subcutaneously since 2015-Nov-21 for renal anaemia. On 2016-Apr-07 the patient developed myocardial infarction after a thyroid gland surgery. The patient died the same day. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-162392 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-063-B004	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-06-24 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral artery occlusion Onset: 2017-06-19 Outcome: recovered	Peripheral artery occlusion / epoetin zeta: not related	Peripheral artery occlusion / epoetin zeta: not assessable	Peripheral artery occlusion / epoetin zeta: listed	Coronary artery disease Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Jun-24 for renal anemia. The current dose was 6000 IU weekly. The batch number of SILAPO was not provided. On 2017-Jun-19 the patient developed embolic occlusion of arteria poplitea left and was hospitalised. An aspiration thrombectomy and angioplasty was performed. The event resolved on 2017-Jun-21 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included coronary heart disease since 2014 and obesity.
DE-STADA-162395 v2.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-063-B004	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-06-24 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2017-10-23 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Coronary artery disease Hypertension Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Jun-24 for renal anemia. The current dose was 9000 IU weekly. The batch number of SILAPO was not provided. On 2017-Oct-23 the patient developed ischaemic stroke and was hospitalised. The patient was discharged on 2017-Nov-17. The event was not resolved. The patient died on 2018-Jan-04 due to bronchitis. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included coronary heart disease since 2014, hypertension arterial since 2000 and obesity. Cross ref.: DE-STADA-162392 (same patient) Follow-up information #1 was received on 2018-Jun-12: The event resolved with sequelae on 2017-Nov-17.
DE-STADA-117806 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-063-B008	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-10-23 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt thrombosis Onset: 2016-02-19 Outcome: recovered	Shunt thrombosis / epoetin zeta: not related	Shunt thrombosis / epoetin zeta: not assessable	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-May-30 and on 2016-May-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2015-Oct-23 for renal anemia. On 2016-Feb-19 the patient developed shunt thrombosis and was hospitalised. The patient underwent shunt revision. The event resolved on 2016-Feb-26 and the patient was discharged. The therapy with SILAPO was not changed. On 2016-Apr-20 the patient died due to infection. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-162497 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-063-B009	60 to 69	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-11-26 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Intravenous bolus	N/A	Myocardial infarction Onset: 2017-04-18 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Nov-26 for renal anemia. The current dose was 18000 IU weekly. Batch number of SILAPO not provided. On 2017-Apr-18 the patient developed myocardial infarction and was hospitalised. The patient received heart catheter, edrug eluting stent and oral platelet aggregation inhibition. The event resolved with sequelae on 2017-Apr-18 and the patient was discharged on 2017-Apr-27. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-202166 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-063-B009	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-26 End: not stated Dosage: 1 x 22000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral embolism Onset: 2018-08-18 Outcome: fatal	Peripheral embolism / epoetin zeta: not related	Peripheral embolism / epoetin zeta: not assessable	Peripheral embolism / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-Jun-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Nov-26 for renal anemia. The current dose was 22000 IU weekly. Batch number of SILAPO was not provided. On 2018-Aug-18 the patient developed arterial embolism of right foot and was hospitalised. The patient died on 2018-Aug-20. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-162497 (same patient).
DE-STADA-100964 v2.0	Yes Patient died Life threatening	DE-063-B013	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-12-29 End: 2015-07-23 Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2015-07-23 Outcome: fatal	Pulmonary embolism / epoetin zeta: not related	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Jul-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 18000 IU weekly subcutaneously since 2014-Dec-29 for renal anemia. On 2015-Jul-21 the patient was hospitalised for re-operation of condition after arm fracture. Two days after operation the patient died due to lung embolism. The reporter assessed the causal relationship between the event and SILAPO as not related. Follow-up information #1 was received on 2016-May-27 and 2016-May-31: The cause of death lung embolism was confirmed. Medical history incided obesity.
DE-STADA-117808 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-063-B016	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-10-23 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-02-11 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-May-30 and on 2016-May-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2015-Oct-23 for renal anemia. On 2016-Feb-11 the patient developed myocardial infarction and died the same day. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-134412 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-065-B005	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-09-25 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2016-07-19 Outcome: recovered	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Sep-25 for renal anemia. The current SILAPO dose was 15000 IU weekly. On 2016-Jul-19 the patient was hospitalised due to ischemic stroke. The patient underwent conservative therapy and the event resolved on 2016-Jul-25. The patient was discharged the same day. The SILAPO dose was increased. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-166880 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-065-B005	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-09-25 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Arterial occlusive disease Onset: 2017-08-10 Outcome: fatal	Arterial occlusive disease / epoetin zeta: not related	Arterial occlusive disease / epoetin zeta: not assessable	Arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jul-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Sep-25 for renal anemia. The current SILAPO dose was 24000 IU weekly. On 2017-Aug-10 the patient developed progressive arterial occlusive disease of both legs. The patient was hospitalised on 2017-Sep-07 and died on 2017-Nov-06 due to progressive arterial occlusive disease and cardial decompensation. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref. DE-STADA-134412 (same patient)
DE-STADA-134348 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-065-B017	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-07-24 End: not stated Dosage: not stated Dosage text: not stated RoA: unknown	N/A	Myocardial infarction Onset: 2016-02-17 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2014-Jul-24 for renal anemia. SILAPO was paused since 2015-Jul-22 because haemoglobin value was in normal range. On 2016-Feb-17 the patient was hospitalised due to myocardial infarction. A cardiac stent was inserted and the event resolved with sequel on 2016-Apr-08. The patient was discharged the same day. The SILAPO administration was finally discontinued on 2015-May-28. The patient changed to another erythropoiesis stimulating substance. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-110273 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-067-B003	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-03-03 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-12-06 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jan-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 10000 IU weekly subcutaneously since 2014-Mar-03 for renal anemia. The current batch was SPO34Q5. On 2015-Dec-06 the patient was hospitalised for myocardial infarction. The patient underwent heart catheter examination and anticoagulation therapy. The event resolved on 2015-Dec-16 and the patient was discharged. Medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-101281 v4.0	Yes Patient died Life threatening	DE-067-B005	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2014-01-24 End: 2015-05-22 Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-06-02 Outcome: fatal	Myocardial infarction / epoetin zeta: possible related	Myocardial infarction / epoetin zeta: possible related	Myocardial infarction / epoetin zeta: listed	Anaemia macrocytic Cerebrovascular accident Cholelithiasis Coronary artery disease Diabetes mellitus Glomerulonephritis Hyperparathyroidism secondary Hypertension Hypertensive heart disease Hyperthyroidism Nephrogenic anaemia Peripheral arterial occlusive disease Renal hypertension Sinus node dysfunction Vasculitis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Aug-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2014-Jan-24 for renal anemia. On 2015-May-25 the patient was hospitalised due to shunt dysfunction and peripheral arterial occlusive disease. On 2015-Jun-02 the patient developed myocardial infarction and died. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up information #1 was received on 2015-Aug-24: The patient died on 2015-Jun-03 due to myocardial infarction. Medical history included pANCA vasculitis (dialysis), glomerulonephritis and peripheral arterial disease with necrosis of toes. Follow-up information #2 was received on 2016-Feb-08: Hospital letter was received. The patient's medical history included amongst other things known coronary 3-vessel disease, hypertensive heart disease, sick sinus syndrome, arterial and renal hypertension, secondary renal hyperparathyroidism, diabetes mellitus, apoplexy in 2006, asymptomatic cholecystolithiasis, hyperchrom macrocytic anemia and latent hyperthyroidism. Follow-up information #3 was received on 2016-Feb-17: The patient received 10000 IU weekly of SILAPO Injektionsloesung in Fertigspritze. The last administered batch was 4V062X402/2017. The last administration before event onset was 2015-May-22.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-102743 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-069-B001	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-01-22 End: 2015-07-27 Dosage: 1 x 5000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2015-08-24 Outcome: fatal	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Atrial fibrillation Basilar artery thrombosis Chronic kidney disease Coronary artery disease Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Pneumonia Prostate cancer Sleep apnoea syndrome	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Aug-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 5000 IU weekly subcutaneously since 2015-Jan-22 for renal anemia. On 2015-Aug-24 the patient was hospitalised with ischemic stroke. At the time of report the event was not resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included hypertension, absoluta arrhythmia with atrial fibrillation, coronary heart disease and basilar vein thrombosis. Additional information was received on 2015-Aug-28 and on 2015-Sep-03. On 2015-Jun-01 the SILAPO dose was changed to 5000 IU weekly. On 2015-Jul-27 the patient received the last SILAPO subcutaneous administration before event onset. The patient was hospitalised for pleuropneumonia from 2015-Jul-28 to 2015-Aug-13. During this hospitalisation the patient suffered from renal and cardiac decompensation which required dialysis. First dialysis after hospitalisation was on 2015-Aug-14 without SILAPO administration. On 2015-Aug-24 the patient developed ischaemic stroke. On 2015-Aug-26 SILAPO was continued intravenously with dialysis. At the time of report the patient was still hospitalised. Further medical history included chronic renal failure, secondary hyperparathyroidism, obstructive sleep apnea and prostatic cancer. Follow-up information #1 was received on 2016-Jun-09: The patient died on 2016-Mar-22. Cause of death was increasing cachexia as consequence of the apoplexy.
DE-STADA-142315 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-069-B010	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2014-05-07 End: 2014-06-10 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Pulmonary embolism Onset: 2014-09-17 Outcome: recovered	Pulmonary embolism / epoetin zeta: not related	Pulmonary embolism / epoetin zeta: not assessable	Pulmonary embolism / epoetin zeta: listed	Breast cancer Chemotherapy Chronic kidney disease Diverticulitis Gastroesophageal reflux disease Hyperlipidaemia Hypertension Hyperuricaemia Hysterectomy Ileus Mediastinitis Nephrogenic anaemia Peritonitis Pulmonary resection Radiotherapy Renal atrophy Rheumatoid arthritis Urge incontinence	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jun-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 IU weekly subcutaneously 2014-May-07 to 2014-Jun-10 for renal anemia. On 2014-Sep-17 the patient was hospitalised due to obstructive small intestine ileus, 4 quatrans peritonitis, mediastinitis and reflux oesophagitis. During the treatment for these events a pulmonary embolism was observed. The patient received surgery, antibiotic treatment, antifungal treatment and anticoagulant therapy regarding the event. The last Silapo administration prior the event was 2014-Jun-10 The outcome was reported to be recovered on 2014-Oct-11 and the patient was discharged the same day. The reporter assessed the causal relationship between the event and SILAPO as not related and it could also be caused by patient's underlying tumour disease and the acute illness. Follow-up information #1 was received on 2017-Jun-26: Hospital letter was received. Medical history included breast cancer, sigmoid diverticulitis, condition after partial lung resection, condition after chemo and radiation therapy, hysterectomy, renal atrophy, chronic renal insufficiency, hypertension, hyperlipidemia, hyperuricemia, hyperliposproteinemia, rheumatoid arthritis and urge incontinence.
DE-STADA-162018 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-069-B012	90 to 99	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-06-27 End: not stated Dosage: 1 x 1500 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2018-01-11 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Atrial fibrillation Cardiac failure Chronic kidney disease Coronary artery disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2016-Jun-27 for renal anemia. The current dose was 1500 IU weekly. The batch number of SILAPO was unknown. On 2018-Jan-11 the patient was hospitalised with unstable angina pectoris (acute coronary syndrome with isolated troponinaemia). The patient received conservative therapy. The patient recovered on 2018-Jan-18 and was discharged. The therapy with SILAPO was continued. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history incuded chronic renal insufficiency, coronary heart disease, cardiac insufficiency, atrial fibrillation and renal anemia.
DE-STADA-190573 v2.0	Yes Other medical important condition	DE-069-B029	70 to 79	Female	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: 2019-10-31 Outcome: not recovered	N/A	N/A	N/A	Acute myeloid leukaemia Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Nov-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2017-Dec-20 for renal anemia. The current dose of SILAPO was 10000 IU subcutaneously weekly. Batch number not provided. Despite increase of SILAPO dose, the haemoglobin decreased. Cause of haemoglobin decrease was the newly diagnosed acute myeloid leukemia in September 2019. At the time of report the event was not resolved. The reporter assessed the causal relationship with SILAPO as not related. Follow-up information #1 was received on 2020-Apr-23: Therapy with SILAPO was continued. The last SILAPO administration before event onset was on 2019-Oct-26.
DE-STADA-104921 v2.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-08-03 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2015-Oct-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2015-May-30 for renal anemia. On 2015-Aug-03 the patient developed severe pain in thorax and left arm and was hospitalised. A myocardial infarction was diagnosed. The patient underwent conservative treatment. The event resolved and the patient was discharged on 2015- Aug-06. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and arteriocoronary bypass. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2016-Oct-25: The patient was hospitalised with anginal attacks and thoracic pain on 2015-Aug-03. Intensive care was performed and the patient received ranolazine. The patient was discharged on 2015-Aug-06 with sequelae. Medical history included also adipositas.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-126455 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2015-07-01 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2015-May-30 for renal anemia. On 2015-Jul-01 the patient developed unstable angina pectoris and was transferred to hospital. The patient received Ranexa (INN: ranolazine). The event resolved on 2015-Jul-03 and the patient was discharged. The SILAPO administration was continued. Patient's medical history included obesity. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921 (same patient). Follow-up information #1 was received on 2016-Oct-25: Patient's medical history included coronary 3-vessel disease, diabetes mellitus, atrial fibrillation, ischemic cardiomyopathy and arteriocoronary bypass.
DE-STADA-126697 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-08-26 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The dose of SILAPO at the time of report was 12000 IU weekly. On 2015-Aug-26 the patient was hospitalised with acute coronary syndrome. A myocardial infarction was diagnosed. Re-instant percutaneous coronary intervention with stent insertion was performed. The patient was discharged on 2015-Sep-09 with sequelae. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455 (same patient).
DE-STADA-126714 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-09-10 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The dose of SILAPO at the time of report was 8000 IU weekly. On 2015-Sep-10 the patient was hospitalised with anginal attacks. A myocardial infarction was diagnosed. Ranolazine was withdrawn and the patient received ISDN. The patient was discharged on 2015-Sep-16 with sequelae. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455, DE-STADA-126697 (same patient).
DE-STADA-126727 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-12-28 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The dose of SILAPO at the time of report was 8000 IU weekly. On 2015-Dec-28 the patient was hospitalised with re-occurrence of thoracic pain. A myocardial infarction was diagnosed. Instant recanalisation was performed. The patient was discharged on 2015-Dec-30 with sequelae. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455, DE-STADA-126697, DE-STADA-126714 (same patient).
DE-STADA-126736 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-02-26 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The dose of SILAPO at the time of report was 8000 IU weekly. On 2016-Feb-26 the patient was hospitalised with acute thoracic pain. A myocardial infarction was diagnosed. Bypass Instant recanalisation and percutaneous coronary intervention was performed. The patient was discharged on 2016-Mar-09 with sequelae. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455, DE-STADA-126697, DE-STADA-126714, DE-STADA-126727 (same patient).
DE-STADA-126740 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-06-16 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Oct-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The dose of SILAPO at the time of report was 8000 IU weekly. On 2016-Jun-16 the patient was hospitalised with thoracic pain. A myocardial infarction was diagnosed. Re-canalisation of ramus circumflexus with percutaneous transluminal coronary angioplasty and therapy change from clopidogrel to prasugrel was performed. The patient was discharged on 2016-Jun-24 with sequelae. The SILAPO administration was continued. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455, DE-STADA-126697, DE-STADA-126714, DE-STADA-126727, DE-STADA-126736 (same patient).
DE-STADA-151725 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-070-B007	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2015-05-30 End: 2016-12-06 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-12-09 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery bypass Coronary artery disease Diabetes mellitus Ischaemic cardiomyopathy Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-May-30 for renal anemia. The last dose of SILAPO was 8000 IU weekly. On 2016-Dec-09 the patient was hospitalised due to recurrent myocardial infarction. The patient was discharged on 2016-Dec-14 for palliative treatment. Due to anamnesis and underlying diseases the patient received conservative treatment. On 2016-Dec-27 the patient died ue to heart insufficiency and cardiomyopathy. The last dose of SILAPO was administered on 2016-Dec-06. Patient's medical history included coronary 3-vessel disease, diabetes mellitus, arteriocoronary bypass, persistent atrial fibrillation, ischemic cardiomyopathy, condition after myocardial infarction and adipositas. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-104921, DE-STADA-126455, DE-STADA-126697, DE-STADA-126714, DE-STADA-126727, DE-STADA-126736, DE-STADA-126740 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-187685 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-075-B027	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-03-27 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2019-02-27 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Cholelithiasis Chronic kidney disease Contrast media allergy Fibroadenoma of breast Glomerulonephritis chronic Hypertension Nephrogenic anaemia Peripheral venous disease Renal transplant Thrombophlebitis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Sep-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2018-Mar-27 for renal anemia. The current dose was 2000 IU weekly. The batch number of SILAPO was unknown. On 2019-Feb-27 the patient was hospitalised with unstable angina pectoris. Therapy of the event was coronary intervention with drug eluting stent intervention. The event resolved on 2019-Mar-03 and the patient was discharged on 2019-Mar-21. The therapy with SILAPO was continued. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history incuded chronic kidney disease stage 4 with chronic glomerulonephritis, kidney transplantation, cholecystolithiasis, fibroadenoma of breast, hypertension arterial, thrombophlebitis, chronic venous insufficiency and allergy to contrast media.
DE-STADA-118443 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-076-B001	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-04-11 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-06-14 Outcome: recovered	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jun-09 and on 2016-Jun-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly, subcutaneously since 2015-Apr-11 for renal anaemia. On 2015-Jun-14 the patient was hospitalised with myocardial infarction. The event resolved on 2015-Jun-27 and the patient was discharged the same day. The reporter assessed the causal relationship between event and SILAPO as not assessable. The patient was also hospitalised from 2015-May-30 to 2015-Jun-27 (reason not reported) and was treated with Erypo FS 4000 in this time. Follow-up information #1 was received on 2018-Dec-06: The batch of the SILAPO product was unknown. No further information was provided.
DE-STADA-151050 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-076-B007	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-04-25 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral infarction Onset: 2017-01-03 Outcome: recovered	Cerebral infarction / epoetin zeta: not related	Cerebral infarction / epoetin zeta: not assessable	Cerebral infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Oct-20. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2015-Apr-25 for renal anemia. On 2017-Jan-03 the patient developed ischaemic stroke. The reporter's causal relationship between event and SILAPO was unknown. No further information was provided. Follow-up information #1 was received on 2018-Dec-06: The patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Apr-25 for renal anemia. The batch of the product was unknown. On 2017-Jan-03 the patient developed cerebral infarction of left middle cerebral artery which required hospitalisation and was life-threatening. The event was treated with medications and resolved on 2017-Jan-14. The patient was discharged the same day. The last SILAPO administration prior to the event was on 2016-Dec-31. The therapy with SILAPO was continued. The reporter's causal relationship between event and SILAPO was assessed as not related. Medical history included obesity.
DE-STADA-118441 v1.0	Yes Patient died Life threatening	DE-076-B008	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-04-14 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2015-06-21 Outcome: fatal	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jun-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 2000 IU weekly subcutaneously since 2015-Apr-14 for renal anaemia. On 2015-Jun-21 the patient was found dead at home, possibly due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not assessable.
DE-STADA-111874 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-077-B003	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-03-11 End: 2015-10-01 Dosage: 1 x 500 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2015-09-21 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Cardiac failure Chronic kidney disease Haemodialysis Hypertensive cardiomyopathy Nephrogenic anaemia Obesity Renal artery stenosis Subarachnoid haemorrhage	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Feb-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 500 IU weekly intravenously since 2015-Mar-11 for renal anemia. The current batch was 4T03ST4. On 2015-Sep-216 the patient was hospitalised with persisting asystole and was hospitalised. After unsuccessful resuscitation the patient died due to myocardial infarction on 2015-Oct-01. Medical history included obesity and subarachnoid bleeding after fall for which the patient was hospitalised from 2015-Jul-22 to 2015-Jul-28. The reporter assessed the causal relationship between event and SILAPO as unrelated. Hospital letter received on 2016-Feb-15: Medical history included chronic renal insufficiency, hemodialysis since January 2014, renal artery stenosis, heart insufficiency, hypertensive cardiomyopathy.
DE-STADA-126945 v3.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-077-B005	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-01-28 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Intravenous bolus	N/A	Myocardial infarction Onset: 2016-08-07 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Nov-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Jan-28 for renal anemia. The dose of SILAPO at the time of report was 24000 IU weekly. On 2016-Aug-07 the patient was hospitalised with myocardial infarction. Bypass insertion was performed. The event resolved on 2016-Aug-08 and the patient was discharged on 2016-Sep-16. The SILAPO administration was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2016-Dec-02: Batch was provided as SY09725. Follow-up information #2 was received on 2017-Aug-18: The route of administration for SILAPO was corrected from subcutaneous to intravenous.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-135424 v6.0	Yes Other medical important condition	DE-077-B005	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-01-28 End: 2016-11-14 Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Drug ineffective Onset: 2016-11-28 Outcome: not recovered Haemoglobin decreased Onset: 2016-11-28 Outcome: recovered	Drug ineffective / epoetin zeta: possible related Haemoglobin decreased / epoetin zeta: possible related	Drug ineffective / epoetin zeta: possible related Haemoglobin decreased / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed Haemoglobin decreased / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2015-Jan-28 for renal anemia. The current dose of SILAPO was 24000 IU intravenously weekly. On 2016-Oct-31 a haemoglobin decrease up to 7.9 g/dl was detected (lack of drug effect). SILAPO was discontinued and the patient was changed to peg epoetin beta. At the time of report the event was not resolved. The reporter assessed the causal relationship between event and SILAPO as possibly related. Cross ref.: DE-STADA-126945 (same patient) Follow-up information #1 was received on 2017-Apr-10 and on 2017-Apr-13: The patient was changed to epoetin from another manufactuerer because despite high dose of Silapo no increase in Hb value was achieved. There was no alternative explanation for decrease of haemoglobin value. Since change to another epoetin the haemoglobin increased to 9.0. According to the reporter the treatment with Silapo was not the cause of haemoglobin value decrease, the haemoglobin value was already decreased before Silapo treatment. Follow-up information #2 was received on 2017-Jul-28: The therapy with SILAPO was discontinued on 2017-May-11. Follow-up information #3 was received on 2017-Aug-18: The administered SILAPO batch was 6503206. The administration before onset was 2016-Nov-14. Follow-up information #4 was received on 2018-Jun-15: The therapy with SILAPO was discontinued on 2016-Nov-14. Follow-up information #5 was received on 2018-Jun-22: The start of event was changed to 2016-Nov-28. The last administration of SILAPO before onset was 2016-Nov-14. SILAPO therapy was discontinued and the patient changed to Mircera (INN: epoetin beta).
DE-STADA-158529 v1.0	Yes Other medical important condition	DE-077-B006	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-03-09 End: 2015-08-14 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Drug ineffective Onset: 2015-08-10 Outcome: recovered	Drug ineffective / epoetin zeta: probable related	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed	Atrial fibrillation Cerebrovascular accident Cerebrovascular disorder Hypertension Iron deficiency Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2015-Mar-09 for renal anemia. The current dose of SILAPO was 8000 IU intravenously weekly and batch: 4X076X4. On 2015-Aug-10 insufficient haemoglobin increase (lack of drug effect) was noted. On 2015-Aug-14 the patient stopped the safety study PASCO II with SILAPO and changed to MIRCERA (INN: epoetin beta). The event resolved on 2015-Sep-07. The reporter assessed the causal relationship with SILAPO as probable related. Medical history included atrial fibrillation, cerebrovascular disease, stroke, hypertension, renal insufficiency since November 2003 and iron deficiency since May 2013.
DE-STADA-142731 v2.0	Yes Other medical important condition	DE-077-B008	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-10 End: 2017-12-12 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Drug ineffective Onset: 2017-12-12 Outcome: recovered Haemoglobin decreased Onset: 2017-12-12 Outcome: recovered	Drug ineffective / epoetin zeta: probable related Haemoglobin decreased / epoetin zeta: probable related	Drug ineffective / epoetin zeta: possible related Haemoglobin decreased / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed Haemoglobin decreased / epoetin zeta: listed	Hyperparathyroidism secondary Hypertension Nephrogenic anaemia Nephrosclerosis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-May-12 (minimum criteria not fulfilled) and on 2017-Jun-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2016-Aug-10 for renal anemia. The current dose of SILAPO was 4000 IU subcutaneously weekly. On 2017-May-11 the patient was discharged from study due to missing haemoglobin increase (lack of drug effect). The patient changed to another erythropoiesis stimulating product (Mircera). The haemoglobin value was 10.1 g/dl at study start and 7.9 g/dl at drop out. After change to another product the haemoglobin increased again up to 10.1 g/dl on 2017-May-08. Medical history included nephrosclerosis, hypertension and secondary hyperparathyroidism. Follow-up information #1 was received on 2018-Mar-29 and on 2018-Apr-03: The report was corrected as follows: On 2017-Dec-12 the patient was discharged from study due to missing haemoglobin increase (lack of drug effect). The haemoglobin values were not reported. The current dose of SILAPO was 12000 IU intravenously weekly and batch no. 70O27P7. The patient changed to another erythropoiesis stimulating product (Mircera) and the event resolved on 2018-Jan-29. The reporter assessed the causal relationship as probable related to SILAPO.
DE-STADA-157819 v4.0	Yes Other medical important condition	DE-077-B010	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-02-09 End: 2017-11-29 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Drug ineffective Onset: 2017-11-27 Outcome: recovered	Drug ineffective / epoetin zeta: probable related	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed	Hyperlipidaemia Hypertension Iron deficiency Nephrogenic anaemia Renal cell carcinoma	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Feb-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2015-Feb-09 for renal anemia. The average dose of SILAPO in the last 3 month was 6000 IU subcutaneously weekly. At the start of treatment the haemoglobin value was 11.9 g/dl. On 2017-Dec-11 the safety study PASCO II with SILAPO was stopped due to insufficient haemoglobin increase (lack of drug effect). The patient was changed to epoetin alfa HEXAL. The outcome of the event was not provided. The causal relationship between event and SILAPO was not provided. Medical history included hyperlipidaemia, hypertension, iron deficiency and and renal cell carcinoma since May 2011. Follow-up information #1 was received on 2018-Mar-09: The current dose of SILAPO was 12000 IU intravenously weekly. Batch number was not provided. On 2017-Nov-27 insufficient haemoglobin increase (lack of drug effect) was noted. On 2017-Nov-27 the patient stopped the safety study PASCO II with SILAPO and changed to epoetin alpha. The event resolved on 2018-Jan-08. The reporter assessed the causal relationship with SILAPO as probable related. Follow-up #2 was generated on 2018-Mar-15 after internal case review in order to fill in the FU medical evaluation for FU#1. Follow-up information #3 was received on 2018-Mar-29 and 2018-Apr-03: The last administration of SILAPO prior to the event was on 2017-Nov-29 and the current batch no. was 70019Q7.
DE-STADA-160762 v1.0	Yes Other medical important condition	DE-077-B012	20 to 29	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-09-04 End: 2017-12-27 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2017-12-27 Outcome: recovered	Drug ineffective / epoetin zeta: probable related	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Apr-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2017-Sep-04 for renal anemia. The current dose of SILAPO was 8000 IU subcutaneously weekly and batch: 70O1B07. On 2017-Dec-27 insufficient haemoglobin increase (lack of drug effect) was noted. On 2017-Dec-27 the patient stopped the safety study PASCO II with SILAPO and changed to MIRCERA (INN: epoetin beta). The last administration of SILAPO was on 2017-Dec-20. The event resolved. The reporter assessed the causal relationship with SILAPO as probable related.
DE-STADA-135979 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-078-B003	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-19 End: 2016-05-11 Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac failure Onset: 2017-02-06 Outcome: fatal Multiple organ dysfunction syndrome Onset: 2017-02-06 Outcome: fatal	Cardiac failure / epoetin zeta: unlikely related Multiple organ dysfunction syndrome / epoetin zeta: unlikely related	Cardiac failure / epoetin zeta: unlikely related Multiple organ dysfunction syndrome / epoetin zeta: unlikely related	Cardiac failure / epoetin zeta: not listed Multiple organ dysfunction syndrome / epoetin zeta: not listed	Alcohol abuse Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-19 for renal anemia. On 2016-May-11 the SILAPO therapy was interrupted. On 2017-Feb-06 the patient developed decompensated heart failure with multiorgan failure. The patient was hospitalised on intensive care unit. The patient died on 2017-Feb-17. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Medical history included obesity and alcohol abuse.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-123572 v2.0	Yes Patient died Life threatening	DE-079-B008	40 to 49	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-02-10 End: 2016-06-16 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cardiac death Onset: 2016-07-01 Outcome: fatal Death Onset: 2016-07-01 Outcome: fatal	Cardiac death / epoetin zeta: unlikely related Death / epoetin zeta: unlikely related	Cardiac death / epoetin zeta: unlikely related Death / epoetin zeta: unlikely related	Cardiac death / epoetin zeta: not listed Death / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Sep-05. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient started receiving SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) (batch: 50047R5) subcutaneously, 6000 IU weekly, for renal anemia on 2016-Feb-10. On 2016-Jun-16 the last dose was administered. On 2016-Jul-02 the patient was found dead in her bed at her nursing home. Acute cardiac death was suspected. The reporter assessed the causality to epoetin zeta as unlikely. Follow-up information #1 was received on 2016-Nov-14: The serious criteria. life-threatening was added. The SILAPO therapy end was 2016-Jun-16 (last administration before onset).
DE-STADA-111395 v2.0	Yes Other medical important condition	DE-079-B002	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-07-16 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	Beloc Zok 95 mg INN: metoprolol Indication: Product used for unknown indication Benalapril 20 mg INN: enalapril Indication: Product used for unknown indication Dekristol 20000 iE INN: cholecalciferol Indication: Product used for unknown indication HCT Hexal 12,5 mg INN: hydrochlorothiazide Indication: Product used for unknown indication Nitrendipin ratiopharm 20 mg INN: nitrendipine Indication: Product used for unknown indication Simvastatin 20 mg INN: simvastatin Indication: Product used for unknown indication	Hypertensive crisis Onset: 2015-12-28 Outcome: unknown	Hypertensive crisis / epoetin zeta: probable related	Hypertensive crisis / epoetin zeta: probable related	Hypertensive crisis / epoetin zeta: listed	Hyperlipidaemia Hyperparathyroidism Hypertension Nephrogenic anaemia Renal tubular acidosis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Feb-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2015-Jul-16 for renal anemia. The current batch of SILAPO was 4X083X4. On 2015-Dec-28 the patient reported about severe increased blood pressure (hypertensive urgency) which was clinically without symptoms. The SILAPO dose was reduced. the outcome of the event was unknown. Medical history included hypertension, hyperparathyroidism, renal acidosis and hyperlipoproteinemia. Concomitant medication was Benalapril 20 mg (INN: enalapril), Beloc Zok 95 mg (INN: metoprolol), Nitrendipin ratiopharm 20 mg (INN: nitrendipine), HCT Hexal 12,5 mg (INN: hydrochlorothiazide), Simvastatin 20 mg, Dekristol 20000 IE (INN: cholecalciferol). The reporter assessed the causal relationship between the event and SILAPO as probably related. Follow-up information #1 was received on 2016-Apr-12: The patient discontinued the study due to the adverse drug reaction.
DE-STADA-177498 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-080-B008	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-12-04 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina pectoris Onset: 2019-02-05 Outcome: recovered Atrial fibrillation Onset: 2019-02-05 Outcome: recovered	Angina pectoris / epoetin zeta: not related Atrial fibrillation / epoetin zeta: not related	Angina pectoris / epoetin zeta: not assessable Atrial fibrillation / epoetin zeta: not assessable	Angina pectoris / epoetin zeta: listed Atrial fibrillation / epoetin zeta: not listed	Atrial fibrillation Coronary angioplasty Coronary artery disease Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2017-Dec-04 for renal anemia. The current dose was 4000 IU weekly. The batch number of SILAPO was unknown. On 2019-Feb-05 the patient was hospitalised with suspicion of angina pectoris and tachyarrhythmia absoluta. The patient was monitored and underwent diagnostic. The events resolved on 2019-Feb-14 and the patient was discharged. The therapy with SILAPO was continued. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history incuded hypertension arterial, arrhythmia absoluta with atrial fibrillation and coronary heart disease and condition after percutaneous transluminal coronary angioplasty.
DE-STADA-131976 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-080-B009	80 to 89	Female	N/A	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Haemorrhagic anaemia Onset: 2016-10-11 Outcome: recovered Small intestinal haemorrhage Onset: 2016-10-11 Outcome: recovered	N/A	N/A	N/A	Atrial fibrillation Cardiac failure Carotid artery occlusion Cerebral artery occlusion Gastrointestinal angiectasia Gastrointestinal haemorrhage Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jan-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) SC 6000.0 iE. from 2016-Sep-08 for renal anaemia. Last treatment before start of AE was on 2016-Oct-11. On 2016-Oct-11 the patient developed haemorrhagic anaemia and small intestinal haemorrhage. The patient was hospitalised and was treated with blood transfusions. The patient recovered and was discharged from hospital on 2016-Oct-18. The reporter assessed the causal relationship with SILAPO as not related. Medical history inlcuded: Insulin-requiring type II diabetes mellitus Arrhythmia absoluta Cardiac insufficiency Occlusion of cerebral arteries Carotid artery occlusion Recurrent Gastrointestinal haemorrhage Gastrointestinal angiectasia at the caecum
DE-STADA-134867 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-080-B011	70 to 79	Male	N/A	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Toe amputation Onset: 2017-02-15 Outcome: recovered Arterial stent insertion Onset: 2017-02-15 Outcome: recovered	N/A	N/A	N/A	Arteriosclerosis Hypertension Insulin-requiring type 2 diabetes mellitus Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Sep-04 for renal anemia. On 2017-Feb-15 the patient was hospitalised for stent surgery of arteria femorals superficialis right and big toe amputation right. The outcome of the event was unknown. The SILAPO dose was not changed. The reporter assessed the causal relationship between event and SILAPO as not related. Add info was provided on 2017-Mar-10: Medical history was provided as insulin-requiring type 2 diabetes mellitus, generalised arteriosclerosis and arterial hypertension; all diagnosed in 2008-Mar and still present. Follow-up information #1 was received on 2017-Sep-27 and on 2017-Sep-28: The patient recovered on 2017-Mar-22 and was discharged the same day. The batch number of the administered SILAPO was not known.
DE-STADA-153455 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-080-B050	70 to 79	Female	N/A	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: 2017-08-16 Outcome: recovered Anaemia Onset: 2017-08-16 Outcome: recovered	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2017-Apr-25 for renal anemia. The current dose of SILAPO was 6000 IU subcutaneously weekly. The batch number was unknown. On 2017-Aug-16 an anaemia of unknown origin with haemoglobin value of 6.0 g/dl was observed lack of drug effect). The patient was hospitalised and received erythrocytes concentrates and the SILAPO dose was increased. The event resolved on 2017-Aug-25 and the patient was discharged. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-118338 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-080-B051	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-10-06 End: not stated Dosage: not stated Dosage text: not stated RoA: unknown	N/A	Intestinal infarction Onset: 2016-05-30 Outcome: fatal	Intestinal infarction / epoetin zeta: not related	Intestinal infarction / epoetin zeta: not assessable	Intestinal infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jun06 and 2016-Jun-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) since 2015-Oct-06 for renal anemia. On 2016-May-30 the patient died due to mesenteric infarction. The reporter assessed the causal relationship between event and SILAPO as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-131964 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-080-B057	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-08 End: 2016-07-20 Dosage: not stated Dosage text: SC 6.000.0 I.E RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2016-07-20 Outcome: recovered	Deep vein thrombosis / epoetin zeta: not related	Deep vein thrombosis / epoetin zeta: not assessable	Deep vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jan-24. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta), SC 6.000.0 I.E. from 2016-Jan-08 until 2016-Jul-20 IU weekly for renal anemia. On 2016-Jul-20 the patient developed deep vein thrombosis of the right leg. The patient received an anticoagulant therapy was initiated with Marcumar (INN: phenprocoumon). The patient was hospitalised. The patient was discharged on 2016-Jul-30. The event was resolved at the time of report. SILAPO treatment was withdrawn on 2016-Jul-20. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included obesity.
DE-STADA-183019 v2.0	Yes Other medical important condition	DE-083-B010	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-06-17 End: 2018-05-16 Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2018-05-16 Outcome: unknown	Drug ineffective / epoetin zeta: probable related	Drug ineffective / epoetin zeta: not assessable	Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jun-25 and 2019-Jun-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jun-17 for renal anemia. The current dose of SILAPO was 8000 IU weekly. Batch number not provided. On 2018-May-16 the patient was switched to Aranesp (INN: darbepoetin alfa) due to lack of drug effect of SILAPO. The outcome was reported to be unknown. The reporter assessed the causal relationship between suspected drug and event as probable related. Follow-up information #1 was received on 2019-Jul-04: After consultation with center, it was stated that SILAPO was not discontinued due to lack of efficacy. The patient became subject to dialysis and therefore treatment was changed to ARANESP. Hb values have been stable under treatment. As no adverse event occurred, this case was nullified.
DE-STADA-183402 v1.0	No	DE-083-B013	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-15 End: 2019-02-27 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Nausea Onset: not stated Outcome: unknown Vomiting Onset: not stated Outcome: unknown	Nausea / epoetin zeta: possible related Vomiting / epoetin zeta: possible related	Nausea / epoetin zeta: possible related Vomiting / epoetin zeta: possible related	Nausea / epoetin zeta: listed Vomiting / epoetin zeta: listed	Hypertension Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jul-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Aug-15 for renal anemia. The current dose of SILAPO was 2000 IU weekly. Batch number not provided. On 2019-Feb-27 SILAPO was discontinued due to nausea and vomiting which occurred twice after SILAPO injection. The haemoglobin value was within normal levels. Medical history included hypertension and type 2 diabetes.
DE-STADA-159278 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-085-B001	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-01 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2018-03-07 Outcome: not recovered	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-01 for renal anemia. The current dose was 4000 IU weekly. The last administered batch was 7002SP7. On 2018-Mar-07 the patient developed somnolence and monoparesis. The patient was hospitalised and ischaemic stroke was diagnosed. The patient was discharged on 2018-Mar-20. The event was not yet resolved. The last SILAPO administration before event was on 2018-Mar-07 and was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-157987 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-085-B003	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-12-14 End: 2018-02-27 Dosage: 1 x 16000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral ischaemia Onset: 2017-03-08 Outcome: recovered	Cerebral ischaemia / epoetin zeta: unlikely related	Cerebral ischaemia / epoetin zeta: not assessable	Cerebral ischaemia / epoetin zeta: listed	Juvenile idiopathic arthritis Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Feb-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-14 for renal anemia. The current dose was 16000 IU weekly. The last administered batch was 6W073X6. On 2017-Mar-08 the patient was hospitalised with suspicion of acute cerebral ischaemia with visual disturbances right. The last SILAPO administration before event was on 2017-Mar-06. The patient underwent conservative therapeutic measures. The event resolved on 2017-Mar-12 and the patient was discharged. Medical history included Juvenile rheumatoid arthritis since 1970. The reporter assessed the causal relationship between event and SILAPO as unlikely related. On 2018-Feb-27 the patient terminated the study at his own request and changed to another Erythropoiesis-Stimulating Agent, ARANESP (INN: darbepoetin alfa).
DE-STADA-177507 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-085-B007	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-01 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-06-27 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-01 for renal anemia. The current dose was 8000 IU weekly and batch: 7O033P7. On 2018-Jun-27 the patient developed myocardial infarction and was hospitalised. The patient underwent intensive care and was discharged on 2018-Jul-20 with sequelae. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-146325 v3.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-085-B008	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-02-02 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Acute myocardial infarction Onset: 2017-07-20 Outcome: fatal	Acute myocardial infarction / epoetin zeta: not related	Acute myocardial infarction / epoetin zeta: not assessable	Acute myocardial infarction / epoetin zeta: listed	Cardiac failure Coronary artery disease Hypertension Nephrogenic anaemia Tobacco abuse	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-14 an on 2017-Aug-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-02 for renal anemia. The current SILAPO dose was 12000 IU weekly. On 2017-Jul-20 the patient died due to acute myocardial infarction. Medical history included coronary heart disease, hypertension, heart insufficiency and tobacco abuse. The reporter assessed the causal relationship as not related to SILAPO. Follow-up information #1 was received on 2017-Sep-22: The batch of last administered SILAPO product was provided: 6x088x6. Follow-up information #2 was received on 2019-Mar-12: The current SILAPO dose was corrected to 9000 IU weekly.
DE-STADA-158122 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-085-B012	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-04 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-12-11 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Deep vein thrombosis Haemorrhage intracranial Hypertension Myocardial infarction Nephrogenic anaemia Renal failure Renal hypertension Renal transplant	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-04 for renal anemia. The current dose was 1500 IU weekly and batch: 7Q054R7. On 2017-Dec-11 the patient developed myocardial infarction and was hospitalised. The event resolved on 2017-Dec-24 and the patient was discharged. The therapy with SILAPO was continued. Medical history included renal insufficiency since 1998, coronary heart disease since December 2015, myocardial infarction in December 2015, deep venous thrombosis lower limbs, hypertension, renal hypertension since 2001, condition after renal transplantation and transplantectomy from January 2008 to June 2009, intracranial bleeding in March 2015. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2019-Mar-12: The current dose was corrected to 15000 IU weekly.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-167339 v2.0	Yes Patient died Life threatening	DE-085-B013	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-02-12 End: not stated Dosage: 1 x 1800 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-05-12 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Aug-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-02 for renal anemia. The current dose was 1800 IU weekly and batch: 70027S7. During a walk on 2018-May-12 the patient suddenly collapsed. The patient was reanimated directly but died due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included obesity. Follow-up information #1 was received on 2019-Mar-12: The batch number was corrected to 70027S7.
DE-STADA-148158 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-086-B010	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-11 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2017-01-06 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Alcohol use Nephrogenic anaemia Overweight	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Nov-11 for renal anemia. Dosage and batch of SILAPO are unknown. On 2017-Jan-06 the patient developed myocardial infarction and was hospitalised. The event resolved the same day. Medical history included renal anemia, overweight, and alcohol consumption. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Nov-21: The patient was hospitalised on 2017-Jan-17 and discharged on 2017-Feb-02. The current dose of SILAPO was 3000 IU weekly intravenously and the therapy was still ongoing. The current batch number o fthe product was unknown. The event did not reoccur.
DE-STADA-172286 v1.0	Yes Life threatening	DE-086-B010	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-11-11 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Transient ischaemic attack Onset: 2016-01-01 Outcome: recovered	Transient ischaemic attack / epoetin zeta: not related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Nov-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Nov-11 for renal anemia. The current dose of SILAPO was 3000 IU weekly intravenously and the therapy was still ongoing. The current batch number o fthe product was unknown. On 20176-Jan-01 the patient developed transient ischaemic attack which resolved the same day. The event did not reoccur. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-148158 (same patient).
DE-STADA-148176 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-086-B012	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-10-28 End: 2017-05-12 Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2017-05-12 Outcome: fatal	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Alcohol use Nephrogenic anaemia Overweight	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Oct-28 for renal anemia. The current SILAPO dose was 9000IU weekly. Since 2017-Apr-10 the patient was hospitalised. On 2017-May-12 the patient died due to ischaemic stroke. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included overweight and alcohol consumption.
DE-STADA-122527 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-089-B004	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-06-27 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2016-07-23 Outcome: not recovered	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: listed	Dialysis Lipoedema Metabolic syndrome Nephrogenic anaemia Obesity Rheumatoid arthritis Stenosis	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Aug-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jun-20 for renal anemia. The current dose of SILAPO was 4000 IU weekly and batch: SZ10225. On 2016-Jul-23 the patient developed shunt occlusion at preexisting stenosis. The patient was hospitalised on 2016-Jul-25. A thrombectomy was performed and hemi-loop and stenosis was removed in elbow. A Palindrom catheter was inserted on 2016-Jul-28. The patient was discharged on 2016-Jul-29. The event was not resolved at the time of report. A catheter change was performed on 2016-Aug-09 due to flow disorders. The therapy with SILAPO was not changed. Medical history included obesity, rheumatoid arthritis, metabolic syndrome and lipedema. The patient received also intermittently corticoids for rheumatoid arthritis and leflunomide which was paused due to breast abscess. The reporter assessed the causal relationship between event and SILAPO as possible related. Follow-up information #1 was received on 2016-Sep-07: Date of first administration of Silapo within the study was changed from 2016-Jun-20 to 2016-Jun-27. Patient started dialysis 3 times a week on 2010-Mar-08. Prior to be included in the PASCO II study the patient already received Silapo (INN: epoetin zeta) 6000 I.U. weekly. Tests performed on 2016-Jun-27 were provided as: haemoglobin 12.7 g/dl, blood pressure 163/96 mmHg, pulse 63 and body weight 136 kg.
DE-STADA-147340 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-089-B009	50 to 59	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-06-20 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-07-05 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease End stage renal disease Nephrogenic anaemia Obesity Tobacco abuse Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jun-20 for renal anemia. The current SILAPO dose was 8000 IU weekly and batch: 6x0844l. On 2017-Jul-05 the patient developed myocardial infarction and was hospitalised. The event resolved the same day. On 2017-Jul-11 an aortocoronary venous bypass was inserted and the patient was discharged on 2017-Jul-24. The SILAPO therapy was not changed. Medical history included end stage renal disease, adipositas, type 2 diabetes mellitus, coronary heart disease, tobacco abuse. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-170276 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-089-B010	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-09-08 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2017-01-14 Outcome: recovered with sequel	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Oct-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) intravenously since 2016-Sep-08 for renal anemia. The current SILAPO dose was 18000 IU weekly and batch: C25131-A919. On 2017-Jan-14 the patient experienced myocardial infarction. The patient was hospitalised and PTCA and Stenting was performed. The patient recovered with sequelae and was discharged on 2017-Jan-23. The SILAPO treatment was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history incuded obesity.
DE-STADA-201520 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-089-B010	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-09-08 End: not stated Dosage: 1 x 20000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2017-10-17 Outcome: fatal	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia Obesity Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-May-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) intravenously since 2016-Sep-08 for renal anemia. The current SILAPO dose was 20000 IU weekly and batch: C25131-A919. On 2017-Oct-17 the patient experienced peripheral arterial occlusive disease Fontaine stage IV . The patient was hospitalised and was treated with wound debridement and antibiosis. The patient was discharged on 2017-Dec-07. The event was not resolved at that time. The SILAPO dose was increased. The patient was again hospitalised on 2017-Dec-29 with phlegmon of foot and died on an unspecified date. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included severe peripheral arterial occlusive disease and obesity. Cross ref.: DE-STADA-170276 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-170272 v1.0	Yes Patient died Life threatening	DE-089-B013	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-06-20 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-06-12 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Oct-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jun-20 for renal anemia. The current SILAPO dose was 4000 IU weekly and batch: 7QS1R7. On 2018-Jun-12 the patient died due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-147167 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-089-B018	50 to 59	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-06-20 End: not stated Dosage: 1 x 10000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2017-07-05 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Coronary artery disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-27. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jun-20 for renal anemia. The current dose was 10000 IU weekly and batch: 6x08407. On 2017-Jul-05 the patient developed exertional dyspnoea on very low level with pulmonary congestion and an unstable angina pectoris was suspected. The patient was hospitalised on 2017-Jul-06 and percutaneous transluminal coronary angioplasty was performed. The patient was discharged on 2017-Jul-10 and the event resolved on 2017-Aug-07. The SILAPO dose was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease.
DE-STADA-147301 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B001	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-18 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2017-08-14 Outcome: fatal Leg amputation Onset: not stated Outcome: fatal	Leg amputation / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not related	Leg amputation / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not assessable	Leg amputation / epoetin zeta: not listed Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Aug-29. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-18 for renal anemia. The current dose was 9000 IU weekly and batch: 6X09526. On 2017-Aug-14 the patient developed progressive peripheral arterial occlusive disease with forefoot phlegmon right. The patient was hospitalised and received antibiotic therapy. In the further course first lower leg then thigh was amputated. The patient died on 2017-Aug-28. The cause of death was septic course after severe peripheral arterial occlusive disease with forefoot phlegmon right. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-153286 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B005	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-18 End: 2017-10-16 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Ischaemic stroke Onset: 2017-10-16 Outcome: fatal	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Dec-18 for renal anemia. The current dose was 6000 IU weekly. On 2017-Oct-16 the patient developed tendency to fall and blurred speech. The patient was hospitalised and ischemic stroke was diagnosed. The patient died on 2017-Oct-17 due to acute cardiac failure, asystolia and suspicion of brain stem infarction. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2017-Oct-16 and the last administered batch was 7OO1507.
DE-STADA-115008 v2.0	Yes Other medical important condition	DE-090-B007	40 to 49	Female	N/A	SILAPO injektionslÃ¶sung in einer Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: 2016-02-01 Outcome: recovered	N/A	N/A	N/A	Lymphoedema Nephrogenic anaemia Obesity Ovarian cancer	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Apr-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) 30000 IU weekly subcutaneously since 2016-Jan-08 for renal anemia. Despite high dose therapy with SILAPO a lack of drug effect was noted. The therapy with SILAPO was withdrawn on 2016-Feb-01. The patient changed to Aranesp (INN: darbepoetin alfa). The event resolved. Medical history included adipositas and lymphedema in legs. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administered batch of SILAPO was 5Q039R5.
DE-STADA-133786 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B011	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-01-20 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2016-09-28 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Feb-21 and on 2017-Feb-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-20 for renal anemia. The current dose was 18000 IU weekly. On 2016-Sep-28 the patient developed unstable angina pectoris. The patient was hospitalised on 2016-Oct-25 and coronary angiography with percutaneous transluminal coronary angioplasty with stent was performed. The event resolved on 2016-Oct-26 and the patient was discharged. The SILAPO dose was not changed. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-157710 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B011	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-01-20 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-01-06 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary angioplasty Coronary artery bypass Coronary artery disease Nephrogenic anaemia Stent placement	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Feb-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-20 for renal anemia. The current dose was 24000 IU weekly. Batch number was not provided. On 2018-Jan-05 the patient was hospitalised with pneumonia. In the due course the patient general condition deteriorated and the patient developed myocardial infarction on 2017-Jan-06. The patient was resuscitated unsuccessfully and died on 2018-Jan-07. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included coronary heart disease and condition after coronary artery bypass surgery and percutaneous transluminal coronary angioplasty with stent placement. Cross ref.: DE-STADA-133786 (same patient).
DE-STADA-163015 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B016	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-19 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2018-03-29 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-19 for renal anemia. The current dose was 6000 IU weekly and batch 7T06977. On 2018-Mar-29 the patient developed peripheral arterial occlusive disease stage IV femoropolliteal with gangrene. The patient was hospitalised and received femoro-popliteal bypass. On 2018-Apr-23 forefoot amputation was performed. The patient was discharged on 2018-May-14. The event resolved with sequelae. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-165790 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B018	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-19 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-06-26 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jul-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-19 for renal anemia. The current dose was 6000 IU weekly. Batch number was not provided. The patietn was hospitalised for sepsis without clear focus on 2018-Jun-24. On 2018-Jun-26 the patient needed reanimation and died due to myocardial infarction. The last administration of SILAPO before the event was on 2018-Jun-23. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included severe peripheral arterial occlusive disease stage IV. Cross ref.: DE-STADA-163015 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-115004 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B017	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-12-09 End: 2016-02-24 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-03-13 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Cerebrovascular accident Coronary artery disease Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Apr-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 12000 IU weekly subcutaneously since 2015-Dec-09 for renal anemia. The patient was hospitalised on 2016-Feb-24 for kidney transplantation. In the beginning of March 2016 the patient had already non-ST-segment elevation myocardial infarction which was treated conservatively. On 2016-Mar-13 the patient developed myocardial infarction and died. Medical history included coronary heart disease and stent-percutaneous transluminal coronary angioplasty, apoplexy and peripheral arterial disease. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2016-Feb-24 and the last administered batch was 5W077W.
DE-STADA-128667 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B020	20 to 29	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-12-11 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2016-11-04 Outcome: fatal	Cerebral haemorrhage / epoetin zeta: unlikely related	Cerebral haemorrhage / epoetin zeta: unlikely related	Cerebral haemorrhage / epoetin zeta: listed	Hypertensive encephalopathy Malignant hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Nov-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-11 for renal anemia. The current dose was 24000 IU weekly. On 2016-Nov-04 the patient was found unconscious at home and was hospitalised. Cerebral hemorrhage was diagnosed. Intensive care was performed. The outcome of the event was unknown. The SILAPO therapy was not changed. Medical history included malignant hypertension with hypertensive encephalopathy. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2017-Feb-14: The patient died on 2017-Jan-09.
DE-STADA-141670 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B021	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-01-20 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2017-05-18 Outcome: recovered	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Atrial fibrillation Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jun-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2016-Jan-20 for renal anemia. The current SILAPO dose was 2000IU weekly. On 2017-May-18 the patient was hospitalised due to ischemic stroke. The patient underwent conservative therapy and the event resolved on 2017-May-22. The patient was discharged the same day. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included: Atrial fibrillation in 2012 Follow-up report #1 was generated on 2018-Jul-31 after internal case review in order to correct the study center and subject number, the initial receive date in the narrative from 2017-Mar-01 to 2017-Jun-14 and the application of SILAPO from intravenous to subcutaneous.
DE-STADA-128668 v2.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-090-B022	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-12-18 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2016-09-08 Outcome: recovered with sequel	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: listed	Brain stem infarction Cerebrovascular accident Hemiparesis Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Nov-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-18 for renal anemia. The current dose was 6000 IU weekly. The patient was hospitalised on 2016-Sep-02 (cause not reported). On 2016-Sep-08 the patient developed hemiataxia left and an ischemic stroke was diagnosed. The patient received anticoagulant therapy and was discharged on 2016-Sep-13. The patient was in rehabilitation clinic until 2016-Nov-30. The event resolved with sequellae. The SILAPO therapy was not changed. Medical history included condition after apoplexy cerebri in 2004 with incomplete hemiparesis left and a brain stem infarction in 2015. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2016-Aug-31 and the last administered batch was 6QO2OR6.
DE-STADA-150773 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B022	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2015-12-18 End: 2017-09-11 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-09-29 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Oct-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-18 for renal anemia. The current dose was 6000 IU weekly. The patient developed myocardial infarction on 2017-Sep-29 during a hospital stay (neurosurgery). The patient received conservative treatment (medication). The patient died on 2017-Oct-01. The last SILAPO administration was on 2017-Sep-11. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-128668 (same patient). Follow-up information #1 was received on 2018-Mar-05: The initial receive date was corrected in the narrative. The last administered batch of SILAPO was 6XO94Z6.
DE-STADA-174085 v3.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B023	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-02-02 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2018-10-11 Outcome: recovered with sequel Peripheral artery occlusion Onset: 2018-10-11 Outcome: recovered with sequel	Peripheral arterial occlusive disease / epoetin zeta: not related Peripheral artery occlusion / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable Peripheral artery occlusion / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed Peripheral artery occlusion / epoetin zeta: not listed	Coronary artery disease Diabetes mellitus Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Dec-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-02 for renal anemia. The current dose was 9000 IU weekly. Batch number was not provided. On 2018-Oct-11 the patient developed peripheral arterial occlusive disease stage IV and occlusion of arteria femoralis superficialis. The patient was hospitalised on 2018-Nov-09 and angiography with percutaneous transluminal angioplasty and stent insertion was conducted. The patient recovered with sequellae and was discharged on 2018-Nov-10. The therapy with SILAPO was continued. The reporter assessed the causal relationship between events and SILAPO as not related. Medical history included coronary heart disease, diabetes mellitus and obesity. Follow-up information #1 was received on 2019-Jan-07: The reporting physician informed that the batch number was not available and cannot be retrieved anymore. Follow-up report #2 was generated on 2019-Jan-11 after internal case review in order to correct the patient's sex in the initial narrative from male to female.
DE-STADA-174620 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B023	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-02-02 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-12-21 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jan-09 and on 2019-Jan-10. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-02 for renal anemia. The current dose was 12000 IU weekly. The reporting physician informed that the batch number was not available and cannot be retrieved anymore. On 2018-Dec-14 the patient was hospitalised for femoralis poplitea bypass surgery at peripheral arterial occlusive disease. On 2018-Dec-21 a non-ST-segment elevation myocardial infarction occurred. In the morning of 2018-Dec-23 the patient collapsed and was found dead in the noon. Cardiopulmonary resuscitation was unsuccessful. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included obesity. Cross reference: DE-STADA-174085 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect druos only)	Company causality (Susoect druos only)	Listedness (Susoect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-134421 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B028	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-24 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial bypass occlusion Onset: 2017-01-15 Outcome: recovered	Arterial bypass occlusion / epoetin zeta: not related	Arterial bypass occlusion / epoetin zeta: not assessable	Arterial bypass occlusion / epoetin zeta: listed	Nephrogenic anaemia Peripheral arterial occlusive disease Peripheral artery bypass	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Mar-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-24 for renal anemia. The current dose of SILAPO was 12000 IU weekly. On 2017-Jan-15 the patient developed acute bypass occlusion at peripheral artery occlusive disease and condition after femoropoplitteal artery bypass right in July 2014. The event resolved on 2017-Jan-17 and the patient was discharged on 2017-Jan-30. The therapy with SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2017-Jan-13 and the last administered batch was 6T043U6.
DE-STADA-153292 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B028	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-24 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Vascular graft occlusion Onset: 2017-10-27 Outcome: recovered Ischaemia Onset: 2017-10-27 Outcome: recovered	Ischaemia / epoetin zeta: not related Vascular graft occlusion / epoetin zeta: not related	Ischaemia / epoetin zeta: not assessable Vascular graft occlusion / epoetin zeta: not assessable	Ischaemia / epoetin zeta: listed Vascular graft occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) since 2015-Dec-24 for renal anemia. The current dose of SILAPO was 8000 IU weekly intravenously. On 2017-Oct-27 the patient developed acrocyanosis and pain right leg. The patient was hospitalised with suspicion of critical ischemia caused by bypass occlusion. Surgery for revision of bypass occlusion of right leg was performed and the event resolved. The patient was discharged on 2017-Nov-20. The therapy with SILAPO was not changed. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-134421 (same patient) The last administration of SILAPO before event was 2017-Oct-23 and the last administered batch was 70O19Q7.
DE-STADA-158185 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B028	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-24 End: 2017-11-25 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2017-11-24 Outcome: recovered Arteriovenous fistula site complication Onset: 2017-11-24 Outcome: recovered	Arteriovenous fistula site complication / epoetin zeta: not related Shunt occlusion / epoetin zeta: not related	Arteriovenous fistula site complication / epoetin zeta: not assessable Shunt occlusion / epoetin zeta: not assessable	Arteriovenous fistula site complication / epoetin zeta: listed Shunt occlusion / epoetin zeta: listed	Coronary artery disease Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) since 2015-Dec-24 for renal anemia. The current dose of SILAPO was 12000 IU weekly subcutaneously and batch: 7O019Q7. On 2017-Nov-25 the patient developed arterio-venous shunt occlusion, stenosis of fistula vein and venous graft limb. The patient was hospitalised and underwent operative shunt revision. The event resolved on 2017-Nov-25 and the patient was discharged on 2017-Nov-28. The therapy with SILAPO was discontinued on 2017-Nov-25. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included coronary heart disease and peripheral arterial occlusive disease since 2009. Cross ref.: DE-STADA-134421, -153292 (same patient).
DE-STADA-178621 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B028	70 to 79	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-24 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Arterial bypass occlusion Onset: 2018-04-20 Outcome: recovered	Arterial bypass occlusion / epoetin zeta: not related	Arterial bypass occlusion / epoetin zeta: not assessable	Arterial bypass occlusion / epoetin zeta: listed	Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-03. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) since 2015-Dec-24 for renal anemia. The current dose of SILAPO was 8000 IU weekly subcutaneously and batch: 7O032P7. On 2018-Apr-20 the patient developed acute femoropoplitteal artery bypass occlusion at peripheral arterial occlusive disease and was hospitalised. A bypass thrombectomy and resection of venous bypass aneurysm was performed. The event resolved and the patient was discharged on 2018-Apr-30. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-134421, -153292, -158185 (same patient).
DE-STADA-114509 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B029	60 to 69	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2015-12-09 End: 2016-02-22 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Intestinal ischaemia Onset: 2016-03-04 Outcome: fatal	Intestinal ischaemia / epoetin zeta: not related	Intestinal ischaemia / epoetin zeta: not assessable	Intestinal ischaemia / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Mar-31. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) 6000 IU weekly subcutaneously since 2015-Dec-09 for renal anemia. On 2016-Feb-26 the patient was hospitalised for bypass surgery for peripheral arterial disease with stenosis of superior mesenteric artery. On 2016-Mar-04 the patient developed acute mesenteric ischemia and died on 2016-Mar-07. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2016-Feb-22 and the last administered batch was 5Q043R5.
DE-STADA-158191 v1.0	Yes Other medical important condition	DE-090-B031	60 to 69	Female	SILAPO injektionslÃ¶sung in einer Fertigspritze INN: epoetin zeta Start: 2015-12-25 End: 2017-06-02 Dosage: 1 x 240000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2017-05-29 Outcome: recovered	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: not assessable	Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) since 2015-Dec-25 for renal anemia. The current dose of SILAPO was 24000 IU weekly subcutaneously and batch: 6WO73X6. Despite high dose therapy with SILAPO a lack of drug effect was noted on 2017-May-29 (haemoglobin between 5.8 and 6.0 mmol/l). The therapy with SILAPO was withdrawn on 2017-Jun-02. The patient changed to Aranesp (INN: darbepoetin alfa). The event resolved. Medical history included adipositas. The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-133807 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B043	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-01-22 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-10-19 Outcome: recovered with sequel Angina unstable Onset: 2016-10-19 Outcome: recovered with sequel	Angina unstable / epoetin zeta: not related Myocardial infarction / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable Myocardial infarction / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Feb-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-22 for renal anemia. The current dose was 8000 IU weekly. On 2016-Oct-19 the patient developed myocardial infarction described as unstable angina pectoris. The patient was hospitalised the same day and coronary angiography was performed. The event resolved with sequel on 2016-Oct-26 and the patient was discharged. The SILAPO dose was not changed. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-160483 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B044	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-01-28 End: 2018-03-22 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2018-03-12 Outcome: fatal	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Apr-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosung in Fertigspritze (INN: epoetin zeta) intravenously since 2016-Jan-28 for renal anemia. The current dose was 6000 IU weekly. On 2018-Mar-12 the patient developed peripheral arterial occlusive disease stage IV with progression of toes gangrene. The last administration of SILAPO was 2018-Feb-03. The patient underwent pelvis-leg angiography with no treatment options (conservative-palliative). The patient died on 2018-Mar-22 and therapy with SILAPO was discontinued. Cause of death was necrotising bursitis olecrani and peripheral arterial occlusive disease stage IV with progression of toes gangrene. The reporter assessed the causal relationship between event and SILAPO as not related.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-153289 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B045	60 to 69	Male	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2015-12-18 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2017-11-22 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Nov-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2015-Dec-18 for renal anemia. The current dose was 4000 IU weekly. On 2017-Nov-17 the patient was hospitalised (cause not provided). On 2017-Nov-22 a peripheral arterial occlusive disease with progression was diagnosed. The patient underwent iliofemoral angiography with percutaneous transluminal angioplasty. The event resolved. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2018-Mar-05: The last administration of SILAPO before event was 2017-Nov-17 and the last administered batch was 7O02407.
DE-STADA-158194 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B051	50 to 59	Male	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2015-12-24 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-09-18 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Myocardial infarction Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2015-Dec-24 for renal anemia. The current dose was 12000 IU weekly and Batch number 6XO89Y6. On 2017-Sep-18 the patient developed myocardial infarction and was hospitalised. Coronary angiography with stent insertion was performed. The event resolved on 2017-Sep-19 and the patient was discharged on 2017-Sep-30. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included coronary heart disease since 2014, peripheral arterial occlusive disease and condition after myocardial infarction in 2014.
DE-STADA-141671 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-090-B053	60 to 69	Male	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2016-02-01 End: not stated Dosage: not stated Dosage text: SC 6.000.0 I.E RoA: Subcutaneous	N/A	Extremity necrosis Onset: 2017-06-02 Outcome: not recovered	Extremity necrosis / epoetin zeta: not related	Extremity necrosis / epoetin zeta: not assessable	Extremity necrosis / epoetin zeta: not listed	Leg amputation Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jun-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient started receiving SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta), SC 6.000.0 I.E. weekly on 2016-Feb-01 for renal anemia. On 2017-Jun-02 the patient suffered from acral necrosis and heel necrosis on the left side. Due to this events the patient was hospitalised from 2017-Jun-06 to 2017-Jun-13. The events were still present. SILAPO treatment was ongoing. Last administration before onset was 2017-May-29. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included well-known severe peripheral arterial occlusion disease, lower leg amputation on the left side.
DE-STADA-163016 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-090-B053	60 to 69	Male	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2016-02-01 End: 2018-04-25 Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-04-25 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-May-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-01 for renal anemia. The current dose was 1000 IU weekly. Batch number was not provided. On 2018-Apr-25 the patient developed myocardial infarction and was hospitalised. Coronary angiography was performed. The patient was discharged on 2018-May-08 and died on 2018-May-16. The last SILAPO administration was on 2018-Apr-25. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref. DE-STADA-141671 (same patient).
DE-STADA-173197 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B003	70 to 79	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2016-01-11 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2018-09-21 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: listed	Carpal tunnel syndrome Cholecystectomy Craniotomy Diabetic nephropathy Gastritis erosive Hyperlipidaemia Hyperparathyroidism secondary Hypertension Left ventricular hypertrophy Meningioma Mitral valve incompetence Nephrogenic anaemia Osteoarthritis Osteopenia Pulmonary oedema Renal cyst Renal failure Restless legs syndrome Scoliosis Thyroidectomy Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Dec-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-11 for renal anemia. The current dose of SILAPO was 8000 IU weekly. Batch number was 7O029Q7. On 2018-Sep-21 the patient developed shunt occlusion and was hospitalised. Shunt revision and thrombectomy was preformed and a new shunt (Gore-Tex) was inserted. The event resolved on 2018-Sep-26 and the patient was discharged on 2018-Oct-01. The therapy with SILAPO was paused. Last administration prior onset was reported as 2018-Sep-17. Medical history included diabetic nephropathy, renal insufficiency, renal cyst, type 2 diabetes mellitus, hyperlipidemia, hypertension, left ventricular hypertrophy, mitral valve insufficiency, lung edema, thyroidectomy, secondary hyperparathyroidism with struma nodosa, erosive gastritis, restless legs snydrome, carpal tunnel syndrome, osteopenia, scoliosis, craniotomy due to meningotheliomatous meningioma, cholecystectomy and gonarthrosis. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-173205 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B003	70 to 79	Female	SILAPO Injektionslösung in Fertigspritze INN: epoetin zeta Start: 2016-01-11 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2018-10-31 Outcome: recovered with sequel Shunt infection Onset: 2018-10-31 Outcome: recovered with sequel	Shunt infection / epoetin zeta: not related Shunt occlusion / epoetin zeta: not related	Shunt infection / epoetin zeta: unlikely related Shunt occlusion / epoetin zeta: unlikely related	Shunt infection / epoetin zeta: not listed Shunt occlusion / epoetin zeta: listed	Carpal tunnel syndrome Cholecystectomy Craniotomy Diabetic nephropathy Gastritis erosive Glomerulonephritis Hyperlipidaemia Hyperparathyroidism secondary Hypertension Left ventricular hypertrophy Meningioma Mitral valve incompetence Nephrogenic anaemia Osteoarthritis Osteopenia Pulmonary oedema Renal cyst Renal failure Restless legs syndrome Scoliosis Thyroidectomy Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Dec-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionslosesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-11 for renal anemia. The current dose of SILAPO was 12000 IU weekly. Batch number was 7O031P7. On 2018-Oct-31 the patient developed shunt occlusion of left forearm with shunt infection and was hospitalised. Abscess removal, shunt suppression and explantation of infected vessel prosthesis was conducted. The event resolved with sequelae on 2018-Nov-05 and the patient was discharged on 2018-Nov-13. The therapy with SILAPO was paused. Last administration prior onset was reported as 2018-Oct-29. Medical history included diabetic nephropathy, renal insufficiency, glomerulonephritis, renal cyst, type 2 diabetes mellitus, hyperlipidemia, hypertension, left ventricular hypertrophy, mitral valve insufficiency, lung edema, thyroidectomy, secondary hyperparathyroidism with struma nodosa, erosive gastritis, restless legs snydrome, carpal tunnel syndrome, osteopenia, scoliosis, craniotomy due to meningotheliomatous meningioma, cholecystectomy and gonarthrosis. The reporter assessed the causal relationship between event and SILAPO as not related. Cross ref.: DE-STADA-173197 (same patient).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-178784 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B009	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-05-11 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2018-12-19 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Arthritis Coronary artery disease Coronary artery stenosis Hyperparathyroidism secondary Hypertension Myocardial infarction Nephrectomy Nephrogenic anaemia Osteoarthritis Peripheral arterial occlusive disease Polyneuropathy Renal failure Tachycardia Transient ischaemic attack Vascular encephalopathy	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-05 and on 2019-Apr-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2016-May-11 for renal anemia. The current dose was 4000 IU weekly and Batch 7O031P7. Patient with known triple vessel disease, arteriosclerosis and stent insertion (2014-Oct-15) developed progress. On 2018-Dec-19 the patient was hospitalised with unstable angina pectoris. The patient received percutaneous coronary intervention with insertion of drug-eluting stent. The patient recovered on 2018-Dec-20 and was discharged on 2018-Dec-21. The therapy with SILAPO was temporary interrupted. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history incuded condition after myocardial infarction, triple vessel disease, stenosis ramus diagonalis, tachycardia, hypertension, renal insufficiency, nephrectomy, transient ischemic attack, subcortal encephalopathy, peripheral arterial occlusive disease, secondary hyperparathyroidism, arthritis, polyneuropathy, gonarthrosis.
DE-STADA-154302 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B010	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-05-17 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2017-11-24 Outcome: recovered	Angina unstable / epoetin zeta: unlikely related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Back pain Chronic gastritis Coronary artery disease Diverticulum intestinal Hepatic cyst Hyperparathyroidism secondary Hypertension Nephrectomy Nephrogenic anaemia Osteoporosis Pancreatic cyst Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Dec-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2016-May-17 for renal anemia. The current dose was 12000 IU weekly and batch: 7O019Q7. On 2017-Nov-24 the patient was hospitalised with unstable angina pectoris (Non-ST-Elevated Myocardial Infarction at known three vessel disease). The patient received percutaneous coronary intervention with drug eluting balloon on 2017-Nov-24. The patient recovered on 2017-Nov-24 and was discharged on 2017-Nov-28. The dose of SILAPO was reduced. The reporter assessed the causal relationship between the event and SILAPO as unlikely related. Medical history incuded renal secondary hyperparathyroidism, osteoporosis, colonic diverticulosis, edematous pangastritis, condition after nephrectomy, lumbar syndrome, arterial hypertension, renal insufficiency, hepatic cysts, pancreatic cysts.
DE-STADA-122341 v2.0	Yes Other medical important condition	DE-091-B014	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-05-10 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2016-07-19 Outcome: recovered	Transient ischaemic attack / epoetin zeta: unlikely related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Cerebral microangiopathy Diabetic nephropathy Haemangioma of spleen Hyperparathyroidism secondary Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Aug-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-10 for renal anemia. The current dose was 12000 IU weekly and batch: 6P011P6. On 2016-Jul-19 the patient developed transient ischemic attack with specific symptoms (personality change with stupor). The event occurred at infection of unknown cause with mild hemoglobin decrease, possibly an erosive gastritis. No therapy for the event was performed. The event resolved 2016-Aug-10. The therapy with SILAPO was increased. Medical history included cerebral microangiopathy since July 2016, secondary hyperparathyroidism since September 2013, spleen hemangioma since November 2012, diabetic nephropathy and renal anemia since June 2013. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2017-Feb-16: The patient died on 2017-Feb-08. Cause of death: food refusal and cachexia, dialyis was stopped on 2017-Feb-05. Death due to myocardial pump failure. No causal relationship to SILAPO.
DE-STADA-158128 v2.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-091-B022	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2016-01-11 End: 2017-11-06 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2017-11-06 Outcome: fatal	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Cardiac failure Cerebrovascular disorder Coronary artery disease Dementia Depression Gastroesophageal reflux disease Haematemesis Hyperlipidaemia Hyperparathyroidism secondary Hypertension Myocardial infarction Nephrogenic anaemia Peripheral arterial occlusive disease Renal failure Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Mar-02. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-11 for renal anemia. The current dose was 4000 IU weekly and batch: 7O024O7. On 2017-Nov-06 the patient developed ischaemic stroke. Due to progressive dementia renouncement of further stroke diagnostic. The patient was discharged on 2017-Nov-07 and received conservative therapy. The study with SILAPO was discontinued on 2017-Dec-13. The last administration before event was 2017-Nov-06. On 2018-Jan-07 the patient developed sudden cardiac death. Medical history included triple vessel disease since January 1980, myocardial infarction, peripheral occlusive disease, cerebrovascular disease, hyperlipidaemia, hypertension, type 2 diabetes mellitus, heart insufficiency, secondary hyperparathyroidism since April 2015, renal insufficiency since March 2014, dementia, depression. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2019-May-22: Additional medical history included reflux esophagitis and haematemesis.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Susoect drugs only)	Company causality (Susoect drugs only)	Listedness (Susoect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-115153 v2.0	Yes Patient died Life threatening	DE-091-B027	80 to 89	Male	Marcumar INN: phenprocoumon Start: 2009-02 End: not stated Dosage: not stated Dosage text: not stated RoA: unknown	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Haemoglobin decreased Onset: 2016-03-05 Outcome: fatal Sepsis Onset: 2016-03-09 Outcome: fatal	Haemoglobin decreased / phenprocoumon: possible related Sepsis / phenprocoumon: unknown	Haemoglobin decreased / phenprocoumon: unknown Sepsis / phenprocoumon: unknown	Haemoglobin decreased / phenprocoumon: not applicable Sepsis / phenprocoumon: not applicable	Atrial fibrillation Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Apr-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Feb-12 for renal anemia. The current dose was 12000 IU weekly and current batch was SV067V5. On 2016-Mar-05 the patient was hospitalised for Marcumar induced bleeding in the left thigh with transfusion requiring hemoglobin decrease. On 2016-Mar-09 the patient developed coma after cerebral seizure. A cranial computer tomography did not reveal any bleeding/ischemia. Due to increased infection and septic state the patient received piperacillin/tazobactam. An intensive care was not conducted due to patient disposal. The patient died on 2016-Mar-15. Medical history included absolute arrhythmia with atrial fibrillation and Marcumar (INN: phenprocoumon) therapy. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2016-Apr-18: The event 'patient died' was changed to 'sepsis at suspicion of pneumonia' on 2016-Mar-09 with fatal outcome. The reporter assessed the causal relationship between event and SILAPO as not related. The initial receive date was corrected in the narrative to 2016-Apr-12.
DE-STADA-121120 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B040	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-06-24 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2016-07-14 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Jul-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 8000 IU weekly subcutaneously since 2016-Jun-24 for renal anaemia. The current batch of SILAPO was bQ024R6. On 2016-Jul-14 the patient developed angina pectoris at preexisting coronary heart disease. Coronary angiography / PCI revealed myocardial infarction with bradycardia. The patient was unsuccessfully reanimated and died the same day. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included chronic atrial fibrillation.
DE-STADA-131420 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B043	70 to 79	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-11-14 End: 2017-01-09 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Intestinal infarction Onset: 2017-01-13 Outcome: fatal Acute abdomen Onset: 2017-01-13 Outcome: fatal	Acute abdomen / epoetin zeta: unlikely related Intestinal infarction / epoetin zeta: unlikely related	Acute abdomen / epoetin zeta: not assessable Intestinal infarction / epoetin zeta: not assessable	Acute abdomen / epoetin zeta: not listed Intestinal infarction / epoetin zeta: listed	Arteriosclerosis Cardiac failure Hypertension Nephrogenic anaemia Non-Hodgkin's lymphoma Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jan-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Nov-14 for renal anemia. The current dose was 4000 IU weekly and batch: 6T043U6. On 2017-Jan-13 the patient developed acute abdomen at mesenteric infarction. The patient underwent laparotomy and postoperative intensive treatment. On 2017-Jan-14 the patient died due to mesenteric infarction. Medical history included dialysis dependent renal insufficiency since 1992, vasosclerosis, hypertension arterial, heart insufficiency, follicular non Hodgkin's lymphoma. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-115143 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-091-B049	80 to 89	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-01-11 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Optic ischaemic neuropathy Onset: 2016-03-07 Outcome: recovered with sequel Visual impairment Onset: 2016-03-07 Outcome: recovered with sequel	Optic ischaemic neuropathy / epoetin zeta: unlikely related Visual impairment / epoetin zeta: unlikely related	Optic ischaemic neuropathy / epoetin zeta: unlikely related Visual impairment / epoetin zeta: unlikely related	Optic ischaemic neuropathy / epoetin zeta: not listed Visual impairment / epoetin zeta: not listed	Nephrogenic anaemia Optic neuropathy	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Apr-12. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Jan-11 for renal anemia. The current dose was 2000 IU weekly and current batch SU064U5. On 2016-Mar-07 the patient developed acute visual impairment with suspicion of acute ischemic optic neuropathy of left eye. The patient was hospitalised on 2016-Mar-11. The patient received therapy with prednisolone. SILAPO therapy was interrupted. The patient was discharged on 2016-Mar-15 and the event resolved with sequelae. Medical history included optic neuropathy right since October 2010. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-170492 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B051	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-05-23 End: 2018-09-26 Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2018-09-26 Outcome: fatal Carotid artery restenosis Onset: 2018-09-26 Outcome: fatal	Carotid artery restenosis / epoetin zeta: unlikely related Ischaemic stroke / epoetin zeta: unlikely related	Carotid artery restenosis / epoetin zeta: not assessable Ischaemic stroke / epoetin zeta: not assessable	Carotid artery restenosis / epoetin zeta: listed Ischaemic stroke / epoetin zeta: listed	Anuria Arteriosclerosis coronary artery Atrial fibrillation End stage renal disease Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Oct-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-23 for renal anemia. The current dose was 12000 IU weekly and batch: 7O029Q7. On 2018-Sep-26 the patient developed left hemispheric ischemia at carotis stenosis and was hospitalised. The patient died on 2018-Sep-27 due to cerebral ischemia at arteria carotis interna stenosis. Medical history included coronary sclerosis, terminal renal insufficiency, anuria and atrial fibrillation. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up report #1 was generated on 2018-Oct-19 after internal case review in order to add the listedness for the event 'carotid artery stenosis'.
DE-STADA-178863 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B074	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-06-21 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Angina unstable Onset: 2019-03-02 Outcome: recovered	Angina unstable / epoetin zeta: not related	Angina unstable / epoetin zeta: not assessable	Angina unstable / epoetin zeta: not listed	Asthma Glucose tolerance impaired Hyperparathyroidism Hypertension Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-05 and on 2019-Apr-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2016-Jun-21 for renal anemia. The current dose was 2000 IU weekly and batch number was T707ET7. On 2019-Mar-02 the patient developed unstable angina pectoris and was hospitalised. Percutaneous coronary intervention with DES insertion was performed on 2019-Mar-06. The event resolved and the patient was discharged. The therapy with SILAPO was increased. The reporter assessed the causal relationship between the event and SILAPO as not related. Medical history incuded prediabetes, hyperparathyroidism, renal insufficiency, bronchial asthma, hypertension.
DE-STADA-177129 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B081	80 to 89	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-05-11 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Thrombosis in device Onset: 2018-12-03 Outcome: recovering	Thrombosis in device / epoetin zeta: not related	Thrombosis in device / epoetin zeta: not assessable	Thrombosis in device / epoetin zeta: listed	Aortic valve incompetence Hyperparathyroidism Hypertension Knee arthroplasty Nephrectomy Nephrogenic anaemia Renal failure	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-11 for renal anemia. The current dose of SILAPO was 12000 IU weekly. Batch number was 7O033P7. On 2018-Dec-03 the patient developed catheter associated thrombus in vena cava superior. The patient was hospitalised on 2019-Jan-16 and the catheter was removed. The patient received anti coagulation therapy with heparin and was discharged on 2019-Jan-25. The event was not yet resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included renal insufficiency, nephrectomy, hypertension, Hyperparathyroidism, knee prosthesis and aortic valve insufficiency.
DE-STADA-165386 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B088	40 to 49	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-05-23 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2018-06-21 Outcome: not recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: listed	Ejection fraction decreased Hyperparathyroidism secondary Nephrectomy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jun-27 and on 2018-Jun-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-23 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was 7Q051S7. On 20198-Jun-21 the patient developed shunt occlusion. Surgial revision was performed during hospitalisation started on 2018-Jun-21. At the time of report the patient was still inpatient and the event wasn't yet resolved. The therapy with SILAPO was paused. Last administration prior onset was reported as 2018-Jun-18. Medical history included condition after nephrectomy on the left in 1999-Jan, secondary hyperparathyroidism since 2008-Dec and mild- to medium-restricted leftventricular pump function since 2014-May. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up report #1 was generated on 2018-Jul-31 after internal case review in order to correct the study center and the serious criteria from 'other medical important' to 'involved ot prolonged inpatient hospitalisation'.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-148505 v1.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-091-B091	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-26 End: not stated Dosage: not stated Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-08-24 Outcome: not recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Alcohol abuse Arteriosclerosis Coronary artery disease Hypercholesterolaemia Hyperphosphataemia Hypertension Nephrogenic anaemia Obesity Type 1 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-11. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Aug-26 for renal anaemia. The current batch of SILAPO was 6XD8BX6. On 2017-Aug-24 the patient was hospitalised due to myocardial infarction. Cardiopulmonary reanimation was performed and percutaneous transluminal coronary angioplasty and stent insertion was carried out. At the time of report the patient was still hospitalised due to concomitant disease (not related to cardiovascular event). SILAPO therapy was interrupted. The last dose of SILAPO was given on 2017-Jul-16. Medical history included obesity, alcohol consumption, severe arteriosclerosis, type 1 diabetes mellitus, hypercholesterolemia, hyperphosphatemia, hypertension and triple vessel disease since January 2008 . The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-169067 v2.0	Yes Life threatening Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-091-B091	50 to 59	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-08-26 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2018-07-18 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Diabetic foot Hyperparathyroidism secondary Myocardial infarction Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Sep-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) 4000 I.U. weekly subcutaneously since 2016-Aug-26 for renal anaemia. Applied batch was provided as 7Q051S7. On 2018-Jul-16 the patient was hospitalised for parathyreoidectomy and hemithyreoidectomy on the left site on 2018-Jul-17. On 2018-Jul-18 postoperative reposition with revision and haematoma clearance in condition after cardiogenic shock in lateral myocardial infarction was performed. Drug eluting stent was placed on ramus circumflex with percutaneous coronary intervention during coronary angiography the same day. SILAPO therapy was paused. The last dose of SILAPO was given on 2018-Jul-13. The patient was discharged on 2018-Sep-13 and the event was recovered. Medical history included secondary hyperparathyroidism since 2002-Apr ongoing, diabetic foot syndrome since 1990-Jan ongoing and triple vessel disease since January 2008 ongoing . Additionally first myocardial infarction already in 2009-Dec followed by multiple infarctions. Severe vessel disease was reported as well. The reporter assessed the causal relationship between event and SILAPO as not related. Cross reference DE-STADA-148505 (same patient) Follow-up information #1 was received on 2018-Oct-30: The event resolved on 2018-Sep-13. Medical history included also obesity.
DE-STADA-178780 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-091-B096	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-07-03 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2019-01-21 Outcome: not recovered	Peripheral arterial occlusive disease / epoetin zeta: not related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Anticoagulant therapy Atrial fibrillation Hyperparathyroidism secondary Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-05 and on 2019-Apr-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Jul-03 for renal anemia. The current dose of SILAPO was 12000 IU weekly. Batch number was 7T076T7. On 2019-Jan-21 the patient developed painful ulceration of lower leg with suspicion of vasculitis. On 2019-Feb-09 the patient was hospitalised with newly diagnosed peripheral arterial occlusive disease. On 2019-Mar-25 the patient was discharged with sequelae. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included secondary hyperparathyroidism and chronic atrial fibrillation treated with anticoagulation therapy with Marcumar (INN: phenprocoumon).
DE-STADA-122334 v1.0	Yes Other medical important condition	DE-091-B101	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-05-16 End: not stated Dosage: 1 x 1000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2016-08-03 Outcome: recovered	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: possible related	Shunt occlusion / epoetin zeta: listed	Depression Hyperparathyroidism secondary Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2016-Aug-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-16 for renal anemia. The current dose of SILAPO was 1000 IU weekly and batch: SW07825. On 2016-Aug-03 the patient developed shunt occlusion. An outpatient thrombectomy was performed and the event resolved the same day. The therapy with SILAPO was reduced. Medical history included obesity, secondary hyperparathyroidism since May 2014 and depression since January 2012. The reporter assessed the causal relationship between event and SILAPO as possible related.
DE-STADA-191790 v2.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B107	90 to 99	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-06-06 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral artery occlusion Onset: 2019-12-02 Outcome: recovering Hemiparesis Onset: 2019-12-02 Outcome: recovering	Cerebral artery occlusion / epoetin zeta: possible related Hemiparesis / epoetin zeta: possible related	Cerebral artery occlusion / epoetin zeta: not assessable Hemiparesis / epoetin zeta: not assessable	Cerebral artery occlusion / epoetin zeta: listed Hemiparesis / epoetin zeta: not listed	Atrial fibrillation Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Dec-09. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Jun-06 for renal anemia. The current SILAPO dose was 4000 IU weekly and Batch: 9SD1S79. On 2019-Dec-02 the patient developed acute occlusion of arteria cerebri media left with hemiparesis right and was hospitalised. The patient underwent intra-arterial lysis therapy and aspiration-thrombectomy. At the time of report the event was improving but the patient was still hospitalised. The reporter assessed the causal relationship between event and SILAPO as possible related. Medical history included paroxysmal atrial fibrillation since May 2013. Follow-up information #1 was received on 2020-Jan-07: The patient was discharged from hospital on 2019-Dec-03 and transferred to neurological rehabilitation. Discharge planned for 2020-Jan-10.
DE-STADA-169867 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-091-B113	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-05-20 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	FERMED INN: iron sucrose Indication: not stated	Shunt thrombosis Onset: 2018-09-26 Outcome: recovered	Shunt thrombosis / epoetin zeta: unlikely related	Shunt thrombosis / epoetin zeta: unlikely related	Shunt thrombosis / epoetin zeta: listed	Hyperparathyroidism secondary Nephrectomy Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Oct-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-20 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was 7T071U7. On 2018-Sep-26 the patient developed shunt thrombosis. The patient was hospitalised. Shunt revision and thrombectomy was performed. The event resolved on 2018-Sep-30 and the patient was discharged. The dose of SILAPO was increased. Medical history included secondary hyperparathyroidism and condition after nephrectomy. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #1 was received on 2018-Oct-29: Relevant concomitant medication was FERMED (INN: iron sucrose).

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-176859 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-091-B113	60 to 69	Female	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-05-20 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2019-02-25 Outcome: recovered	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: unlikely related	Shunt occlusion / epoetin zeta: listed	Aortic arteriosclerosis Hyperparathyroidism secondary Hypertension Hysterectomy Nephrectomy Nephrogenic anaemia Obesity Peripheral arterial occlusive disease Shunt occlusion Thyroidectomy Toe amputation Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-05 and on 2019-Apr-06. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-May-20 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was 77076T7. On 2019-Feb-25 the patient developed shunt occlusion. The patient was hospitalised. Shunt revision, thrombectomy and stent insertion was performed. The event resolved on 2019-Feb-26 and the patient was discharged on 2019-Mar-05. The dose of SILAPO was increased. Medical history included multiple surgeries of shunt arm and shunt occlusion, type 2 diabetes mellitus, secondary hyperparathyroidism, condition after nephrectomy, peripheral arterial occlusive disease, amputation of toes, abdominal aortic sclerosis, hysterectomy, thyroidectomy, hypertension, adipositas. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Cross ref.: DE-STADA-169867 (same patient).
DE-STADA-154304 v2.0	Yes Life threatening	DE-091-B123	60 to 69	Female	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug effect decreased Onset: 2017-10-21 Outcome: not recovered	N/A	N/A	N/A	Arthralgia Depression Diabetes mellitus Gastrinoma Meniscus injury Nephrectomy Nephrogenic anaemia Pancreatic carcinoma metastatic Renal cell carcinoma Restless legs syndrome Somatic symptom disorder	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Sep-25 and on 2017-Dec-13. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2016-May-17 for renal anemia. The current dose of SILAPO was 30000 IU subcutaneously weekly. The last administered batch was 7O006O7. On 2017-Oct-24 a decreased effect at metastatic tumor (pancreas neoplasm with liver and lung metastasis), tumor anemia at high C reactive protein and procalcitonin and iron deficiency was detected. The patient refused any diagnostic and therapy. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included restless leg syndrome, somatisation disorder, suspicion of gastrinoma, diabetes with pathologic glucose tolerance test, gonalgia, depression, meniscus lesion. Follow-up information #1 was received on 2018-Mar-02: The patient still suffered from lack of drug effect since 2017-Oct-21. Meanwhile a histologic examination revealed renal cell carcinoma. The patient received Sunitinib since 2018-Feb-21. The last administration of SILAPO prior to the event was 2017-Oct-21. Medical history included also condition after renal cell carcinoma and nephrectomy right in 2001 and left in October 2007.
DE-STADA-141294 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-093-B004	70 to 79	Male	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2016-03-15 End: 2017-05-06 Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Peripheral arterial occlusive disease Onset: 2017-04 Outcome: fatal Calciphylaxis Onset: 2017-03-28 Outcome: fatal Leg amputation Onset: 2017-04-18 Outcome: fatal Sepsis Onset: 2017-04 Outcome: fatal	Calciphylaxis / epoetin zeta: not related Leg amputation / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not related Sepsis / epoetin zeta: not related	Calciphylaxis / epoetin zeta: not related Leg amputation / epoetin zeta: not related Peripheral arterial occlusive disease / epoetin zeta: not assessable Sepsis / epoetin zeta: not related	Calciphylaxis / epoetin zeta: not listed Leg amputation / epoetin zeta: not listed Peripheral arterial occlusive disease / epoetin zeta: not listed Sepsis / epoetin zeta: not listed	Cerebral infarction Chronic kidney disease Chronic obstructive pulmonary disease Colon cancer Hyperparathyroidism Hyperuricaemia Nephrogenic anaemia Polyarthritis Pulmonary hypertension Renal hypertension Sleep apnoea syndrome Tachycardia paroxysmal Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Jun-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Mar-15 for renal anemia. The current dose was 3000 IU weekly. On 2017-Mar-28 the patient was diagnosed with calciphylaxis of right thigh. Then the patient developed severe peripheral arterial occlusive disease with amputation of left thigh on 2017-Apr-18. The patient developed sepsis due to wound infection and died on 2017-May-06. Patient's medical history included paroxysmal tachycardia, polyarthritis, chronic renal disease, renal hypertension, renal hyperparathyroidism, secondary hyperuricemia, type 2 diabetes mellitus, COPD, sleep apnoea syndrome, pulmonary hypertension, colon carcinoma in 1998 and cerebral infarction in 2011. The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-153558 v2.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-094-B009	60 to 69	Male	acetylsalicylic acid INN: acetylsalicylic acid Start: not stated End: not stated Dosage: not stated Dosage text: not stated RoA: unknown clopidogrel INN: clopidogrel Start: not stated End: not stated Dosage: not stated Dosage text: not stated RoA: unknown SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Start: 2017-06-29 End: 2017-08-26 Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebral haemorrhage Onset: 2017-09-06 Outcome: fatal	Cerebral haemorrhage / acetylsalicylic acid: unknown Cerebral haemorrhage / clopidogrel: unknown Cerebral haemorrhage / epoetin zeta: unlikely related	Cerebral haemorrhage / acetylsalicylic acid: possible related Cerebral haemorrhage / clopidogrel: possible related Cerebral haemorrhage / epoetin zeta: unlikely related	Cerebral haemorrhage / acetylsalicylic acid: listed Cerebral haemorrhage / clopidogrel: listed Cerebral haemorrhage / epoetin zeta: not listed	Coronary artery disease Hypertension Ischaemic cardiomyopathy Nephrogenic anaemia Peripheral arterial occlusive disease Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Dec-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Jun-29 for renal anemia. The current dose was 3000 IU weekly. The patient died due to myocardial infarction on 2017-Sep-05. Medical history included coronary heart disease, hypertension, type 2 diabetes mellitus and heart insufficiency. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2017-Dec-13: The report was modified. The current dose of SILAPO was 6000 IU subcutaneously weekly. The last administered batch was LX098ZB. On 2017-Sep-06 the patient developed hemorrhage intracerebral at administration of acetylsalicylic acid and clopidogrel. The patient was hospitalised and received ventricle drainage. The patient died on 2017-Sep-09 due to hemorrhage intracerebral. The therapy with SILAPO discontinued on 2017-Aug-26. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease, ischemic cardiomyopathy, type 2 diabetes mellitus, arterial hypertension and peripheral arterial occlusive disease.
DE-STADA-179768 v2.0	Yes Other medical important condition	DE-094-B012	70 to 79	Female	N/A	SILAPO Injektionsloesung in Fertigspritze INN: epoetin zeta Indication: Nephrogenic anaemia	Drug ineffective Onset: not stated Outcome: unknown	N/A	N/A	N/A	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2017-Jun-29 for renal anemia. The current dose of SILAPO was 24000 IU subcutaneously weekly. Batch was not available. On an unknown date the patient developed inadequate hemoglobin increase, hyperregenerative anemia, haemorrhagic anemia (lack of drug effect). Erythropoetin specific antibodies were excluded. The therapy with SILAPO was continued. The outcome of the event was unknown. The reporter assessed the causal relationship with SILAPO as not related. Follow-up information #1 was received on 2019-Apr-29: The conducted test for exclusion of Erythropoetin specific antibodies was an anti erythropoietin antibodies lab test.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect druos only)	Company causality (Suspect druos only)	Listedness (Suspect druos only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-197877 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-094-B012	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-06-29 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2020-02-09 Outcome: fatal	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-Mar-27 and on 2020-Mar-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2017-Jun-29 for renal anemia. The current dose of SILAPO was 24000 IU subcutaneously weekly. Batch number was not available. On 2020-Feb-09 the patient was hospitalised with slurred speech. In hospital an ischaemic stroke was diagnosed. The patient died on 2020-Feb-21. Last administration of SILAPO prior to the event was 2020-Feb-08. The reporter assessed the causal relationship with SILAPO as unlikely related. Medical history included obesity. Cross ref.: DE-STADA-179768 (same patient).
DE-STADA-153557 v3.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-094-B014	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-02-22 End: 2017-10-26 Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-10-26 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Coronary artery disease Hypertension Nephrogenic anaemia Peripheral arterial occlusive disease	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2017-Dec-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Feb-22 for renal anemia. The current dose was 2000 IU weekly. The patient died due to myocardial infarction on 2017-Nov-03. Medical history included coronary heart disease, atrial fibrillation, peripheral occlusive disease and hypertension. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up information #1 was received on 2017-Dec-08: The patient developed myocardial infarction at home on 2017-Oct-26. The patient was hospitalised. The outcome of the event was fatal. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Follow-up information #2 was received on 2018-Apr-18: The last administration of SILAPO prior to the event was on 2017-Oct-20. The therapy with SILAPO was discontinued on 2017-Oct-26.
DE-STADA-179623 v1.0	Yes Life threatening Involved or prolonged inpatient hospitalisation	DE-094-B035	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2016-12-30 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2019-03-14 Outcome: recovered	Ischaemic stroke / epoetin zeta: unlikely related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Atrial fibrillation Cerebrovascular accident Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2016-Dec-31 for renal anemia. The current dose was 12000 IU weekly. Batch number not provided. On 2019-Mar-14 the patient developed acute hemiparesis and aphasia during dialysis. The patient was hospitalised with ischaemic stroke. The event was treated with acetylsalicylic acid and the patient was discharged on 2019-Mar-29. The event resolved on 2019-Mar-30. The therapy with SILAPO was interrupted. Medical history included stroke and paroxysmal atrial fibrillation. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-165140 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-094-B039	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-02-14 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2017-12-07 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jun-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2017-Feb-14 for renal anemia. The current dose was 6000 IU weekly. On 2017-Dec-07 the patient was hospitalised for stent placement for peripheral arterial occlusive disease in the left leg On 2017-Dec-21 he was discharged and the event resolved. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely.
DE-STADA-179628 v1.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-094-B057	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-10-03 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Cerebrovascular accident Onset: 2019-04-07 Outcome: fatal	Cerebrovascular accident / epoetin zeta: unlikely related	Cerebrovascular accident / epoetin zeta: not assessable	Cerebrovascular accident / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Oct-03 for renal anemia. The current dose was 4000 IU weekly. Batch number not provided. On 2019-Apr-07 the patient developed unspecified stroke. The patient was hospitalised and despite intensive medicinal measures the patient died on 2019-Apr-14. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-165135 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-094-B062	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-02-15 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2018-02-08 Outcome: recovered	Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Peripheral arterial occlusive disease / epoetin zeta: not assessable	Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jun-26. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2017-Feb-15 for renal anemia. The current dose was 6000 IU weekly. On 2018-Feb-08 the patient was hospitalised for femoralis stent placement for peripheral arterial occlusive disease in the left leg On 2018-Feb-15 he was discharged and the event resolved. The SILAPO therapy was not changed. The reporter assessed the causal relationship between event and SILAPO as unlikely.
DE-STADA-178126 v1.0	Yes Patient died Life threatening	DE-098-B011	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-12-29 End: not stated Dosage: 1 x 9000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Myocardial infarction Onset: 2019-03-11 Outcome: fatal	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-22. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2017-Dec-29 for renal anemia. The current dose was 9000 IU intravenously weekly., Batch 80OO7T8. On 2019-Mar-11 the patient died due to myocardial infarction. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included obesity.
DE-STADA-155065 v3.0	Yes Patient died Life threatening Involved or prolonged inpatient hospitalisation	DE-100-B021	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2017-04-12 End: 2017-11-21 Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2017-11-20 Outcome: fatal	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Cardiac failure Coronary artery disease Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2018-Jan-01. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2017-Apr-12 for renal anemia. The current dose was 4000 IU weekly. On 2017-Nov-20 the patient developed myocardial infarction at known coronary heart disease with decompensated heart insufficiency and was hospitalised on 2017-Nov-21. The SILAPO therapy was interrupted on 2017-Nov-21. At the time of report the event was not resolved. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included coronary heart disease and hypertension arterial. Follow-up information #1 was received on 2018-Feb-16: The patient died on 2018-Jan-02 due to acute myocardial infarction and acute renal failure. These events were not suspected as adverse events of SILAPO. Follow-up information #2 was received on 2018-May-02: The serious criteria was updated to 'patient died' and 'life-threatening'. The outcome of the event was fatal.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-180376 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B022	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-11-01 End: not stated Dosage: 1 x 12000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2019-04-29 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Coronary artery disease Hypertension Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-07. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Nov-01 for renal anemia. The current dose was 12000 IU weekly. Batch not provided. On 2019-Apr-29 the patient developed myocardial infarction and was hospitalised. The event resolved on 2019-May-03 and the patient was discharged. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included type 2 diabetes mellitus, hypertension and coronary heart disease.
DE-STADA-180921 v1.0	Yes Patient died Involved or prolonged inpatient hospitalisation	DE-102-B027	80 to 89	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-12-21 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Deep vein thrombosis Onset: 2019-04-25 Outcome: unknown Septic shock Onset: 2019-04-25 Outcome: fatal	Deep vein thrombosis / epoetin zeta: not related Septic shock / epoetin zeta: not related	Deep vein thrombosis / epoetin zeta: not assessable Septic shock / epoetin zeta: not related	Deep vein thrombosis / epoetin zeta: listed Septic shock / epoetin zeta: not listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-15. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Dec-21 for renal anemia. The current dose was 15000 IU weekly. Batch not provided. On 2019-Apr-25 the patient developed deep vein thrombosis femoral and septic shock and was hospitalised. The patient died on 2019-Apr-27 due to septic shock and renal failure. The reporter assessed the causal relationship between the events and SILAPO as not related. Medical history included hypertension.
DE-STADA-181548 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B041	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-12-03 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2019-05-18 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Hypertension Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Dec-03 for renal anemia. The current dose was 24000 IU weekly. Batch not provided. On 2019-May-18 the patient developed myocardial infarction and was hospitalised. A stent insertion was performed and the event resolved on 2019-May-21. The patient was discharged. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included type 2 diabetes mellitus, and hypertension.
DE-STADA-177647 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B048	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-06-15 End: not stated Dosage: 1 x 18000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2019-02-01 Outcome: recovered	Myocardial infarction / epoetin zeta: not related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Atrial fibrillation Hypertension Nephrogenic anaemia Type 2 diabetes mellitus	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-14. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Jun-15 for renal anemia. The current dose was 18000 IU weekly. Batch not provided. On 2019-Feb-01 the patient developed myocardial infarction and was hospitalised. The patient received conservative therapy. The event resolved on 2019-Feb-08 and the patient was discharged. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not related. Medical history included type 2 diabetes mellitus, hypertension and atrial fibrillation.
DE-STADA-180130 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B067	60 to 69	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-05-16 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Transient ischaemic attack Onset: 2019-04-18 Outcome: recovered	Transient ischaemic attack / epoetin zeta: not related	Transient ischaemic attack / epoetin zeta: not assessable	Transient ischaemic attack / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-30. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-May-16 for renal anemia. The current dose was 24000 IU weekly, batch no. not provided. On 2019-Apr-18 the patient was hospitalised with transient ischaemic attack of media stroma area. The event resolved on 2019-Apr-20 spontaneously and the patient was discharged. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-182792 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B071	70 to 79	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-09-05 End: not stated Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Coronary artery disease Onset: 2019-05-07 Outcome: recovered	Coronary artery disease / epoetin zeta: not related	Coronary artery disease / epoetin zeta: not assessable	Coronary artery disease / epoetin zeta: not listed	Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jun-21. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously weekly since 2018-Sep-05 for renal anemia. The current dose was 24000 IU weekly. On 2019-May-07 he suffered from coronay heart disease in two vessels. He received stent implantation due to the event. The outcome was reported to be recovered on 2019-May-10. The patient was in-patient from 2019-May-07 to 2019-May-10. The Silapo treatment wasn't changed. Medical history was reported as ongoing hypertension arterial The reporter assessed the causal relationship between the event and SILAPO as not related.
DE-STADA-178311 v2.0	Yes Involved or prolonged inpatient hospitalisation	DE-102-B080	70 to 79	Female	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-04-27 End: not stated Dosage: 1 x 15000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Ischaemic stroke Onset: 2019-02-19 Outcome: recovered	Ischaemic stroke / epoetin zeta: not related	Ischaemic stroke / epoetin zeta: not assessable	Ischaemic stroke / epoetin zeta: listed	Alcohol abuse Atrial fibrillation Hypertension Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Mar-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Apr-27 for renal anemia. The current dose was 15000 IU weekly, batch no. not provided. On 2019-Feb-19 the patient developed ischemic stroke and was hospitalised. The event resolved on 2019-Mar-18 and the patient was discharged. The SILAPO therapy was continued. Medical history included hypertension atrial fibrillation and alcohol consumption. The reporter assessed the causal relationship between event and SILAPO as not related. Follow-up report #1 was generated on 2019-May-02 after internal case review in order to delete the end date of SILAPO administration.
DE-STADA-182604 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-117-B008	80 to 89	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2019-01-07 End: not stated Dosage: 1 x 3000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Myocardial infarction Onset: 2019-03 Outcome: recovered	Myocardial infarction / epoetin zeta: unlikely related	Myocardial infarction / epoetin zeta: not assessable	Myocardial infarction / epoetin zeta: listed	Nephrogenic anaemia Pneumonia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Jun-17. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2019-Jan-07 for renal anaemia. The current dose was 3000 IU weekly. Batch not provided. On 2019-Mar-14 the patient experienced myocardial infarction and was hospitalised. The patient received 300mg clopidogrel. The event resolved on 2019-Apr-04 and the patient was discharged. The SILAPO therapy was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely. Medical history included renal anaemia, bronchopneumonia.
DE-STADA-182608 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-117-B016	60 to 69	Male	SILAPO Injektionslosesung in Fertigspritze INN: epoetin zeta Start: 2018-06-08 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt thrombosis Onset: 2019-03-30 Outcome: recovered	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously for renal anaemia since 2018-Jun-08. The current dose was 4000 IE. Batch 77076T7. On 2019-Mar-30 the patient developed shunt thrombosis and was hospitalised. A thrombectomy was performed on 2019-Apr-05. The event resolved on 2019-Apr-08. The patient was discharged. The SILAPO treatment was continued. The reporter assessed the causal relationship between event and SILAPO as possible. Medical history included renal anaemia.

ICSR No.	Seriousness	Patient ID	Patient age cohort	Patient sex	Suspect drugs	Concomitant drugs	Events [PT] (MedDRA v23.0)	Reporter causality (Suspect drugs only)	Company causality (Suspect drugs only)	Listedness (Suspect drugs only)	Medical history episodes [PT] (MedDRA v23.0)	Narrative
DE-STADA-182612 v1.0	Yes Other medical important condition	DE-117-B018	60 to 69	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-06-08 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Shunt thrombosis Onset: 2019-03-19 Outcome: recovered	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: possible related	Shunt thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-May-28. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia Linked to DE-STADA-182608, same patient. A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously for renal anaemia since 2018-Jun-08. The current dose was 4000 IE. Batch 7VD83X7. On 2019-Mar-19 the patient developed shunt thrombosis. The patient received acetylsalicylic acid 100 mg orally and FRAGMIN P FORTE (INN: dalteparin) sc. The event resolved on 2019-Mar-23. The SILAPO treatment was continued. The reporter assessed the causal relationship between event and SILAPO as possible. Medical history included renal anemia.
DE-STADA-187744 v2.0	Yes Other medical important condition	DE-117-B017	50 to 59	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2019-04-22 End: 2019-09-16 Dosage: 1 x 24000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Drug ineffective Onset: 2019-09-18 Outcome: recovering	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: possible related	Drug ineffective / epoetin zeta: listed	Nephrogenic anaemia Obesity	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Sep-25. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) since 2019-Apr-22 for renal anemia. The current dose of SILAPO was 24000 IU subcutaneously weekly and batch: 8Z050b9. Despite 24000 IU of SILAPO weekly there was inadequate low haemoglobin concentration (lack of drug effect) noted on 2019-Sep-18. SILAPO was withdrawn on 2019-Sep-23 and patient changed to another erythropoietin product NEORECORMON 5000 (INN: epoetin beta). The last administration of SILAPO was on 2019-Sep-16. At the time of report the event was not resolved. The reporter assessed the causal relationship with SILAPO as possible. Patient's medical history included obesity. Follow-up information #1 was received on 2019-Oct-22: After change to another erythropoietin product the hemoglobin level increased from 6.8 to 7.8 g/dl on 2019-Oct-07.
DE-STADA-193040 v1.0	Yes Involved persistence of significant disability or incapacity Involved or prolonged inpatient hospitalisation	DE-117-B018	80 to 89	Female	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-10-18 End: not stated Dosage: 1 x 2000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Peripheral arterial occlusive disease Onset: 2019-12-20 Outcome: recovered with sequel Arterial thrombosis Onset: 2019-12-20 Outcome: recovered with sequel	Arterial thrombosis / epoetin zeta: unlikely related Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Arterial thrombosis / epoetin zeta: unlikely related Peripheral arterial occlusive disease / epoetin zeta: unlikely related	Arterial thrombosis / epoetin zeta: listed Peripheral arterial occlusive disease / epoetin zeta: not listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-Jan-08. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A female patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) intravenously since 2018-Oct-18 for renal anemia. The current dose of SILAPO was 2000 IU weekly. Batch number was BWO28X8. On 2019-Dec-20 the patient developed peripheral arterial occlusive disease with arterial thrombosis and was hospitalised. The patient underwent thrombectomy and lysis. The event resolved with sequelae on 2019-Dec-27 and the patient was discharged on 2019-Dec-30. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-179634 v2.0	Yes Involved persistence of significant disability or incapacity	DE-117-B021	50 to 59	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-10-09 End: not stated Dosage: 1 x 6000 IU per every 1 Week Dosage text: not stated RoA: Intravenous (nos)	N/A	Thrombophlebitis superficial Onset: 2019-03-15 Outcome: recovered with sequel	Thrombophlebitis superficial / epoetin zeta: unlikely related	Thrombophlebitis superficial / epoetin zeta: not assessable	Thrombophlebitis superficial / epoetin zeta: listed	Microscopic polyangiitis Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Apr-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Oct-09 for renal anemia. The current dose of SILAPO was 6000 IU weekly. Batch number was 7T076T7. On 2019-Mar-15 the patient developed thrombophlebitis of left lower leg (superficial vein, no deep leg vein thrombosis). The event was treated with Fragmin P Forte subcutaneously daily. The event resolved with sequelae on 2019-Apr-22. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related. Medical history included microscopic polyangiitis. Follow-up information #1 was received on 2019-Apr-26: The report confirmed that this report was not life-threatening. Furthermore the application of SILAPO was corrected from subcutaneously to intravenously.
DE-STADA-189403 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-120-B003	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-11-05 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2019-10-21 Outcome: recovered	Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Oct-23. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Nov-05 for renal anemia. The current dose of SILAPO was 8000 IU weekly. Batch number was 8z04309. On 2019-Oct-21 the patient developed shunt occlusion and was hospitalised. A shunt revision was performed and the patient was discharged on 2019-Oct-23. The event resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related.
DE-STADA-196526 v1.0	Yes Other medical important condition	DE-120-B005	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-11-05 End: not stated Dosage: 1 x 8000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Subclavian vein thrombosis Onset: 2019-12-29 Outcome: recovered	Subclavian vein thrombosis / epoetin zeta: unlikely related	Subclavian vein thrombosis / epoetin zeta: not assessable	Subclavian vein thrombosis / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2020-Mar-04. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Nov-05 for renal anemia. The current dose of SILAPO was 8000 IU weekly. Batch number not provided. On 2019-Dec-29 the patient developed subclavian vein thrombosis right. The patient received anticoagulation therapy and the event resolved on 2020-Feb-21 The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as unlikely related.
DE-STADA-176482 v1.0	Yes Involved or prolonged inpatient hospitalisation	DE-120-B007	80 to 89	Male	SILAPO Injektionslosung in Fertigspritze INN: epoetin zeta Start: 2018-11-19 End: not stated Dosage: 1 x 4000 IU per every 1 Week Dosage text: not stated RoA: Subcutaneous	N/A	Shunt occlusion Onset: 2019-02-11 Outcome: not recovered	Shunt occlusion / epoetin zeta: not related	Shunt occlusion / epoetin zeta: not assessable	Shunt occlusion / epoetin zeta: listed	Nephrogenic anaemia	This report was received via a physician from the post-authorisation safety study PASCO II (PMS-830-09-0082) with SILAPO (INN: epoetin zeta) on 2019-Feb-18. Study name: PASCO II - SILAPO administered SC for treatment of renal anemia A male patient received SILAPO Injektionsloesung in Fertigspritze (INN: epoetin zeta) subcutaneously since 2018-Nov-19 for renal anemia. The current dose of SILAPO was 4000 IU weekly. Batch number was 7OO33P7. On 2019-Feb-11 the patient developed relapse of thrombotic shunt occlusion and was hospitalised. Atrial catheter was inserted. The patient was discharged on 2019-Feb-14. The event was not yet resolved. The therapy with SILAPO was continued. The reporter assessed the causal relationship between event and SILAPO as not related.

	Statistic	Retacrit (N = 4496)	Silapo (N = 1841)	Total (N = 6337)
Exposure to Epoetin Zeta (in days)				
	n	4496	1841	6337
	Mean (SD)	681.7 (396.51)	629.0 (380.03)	666.4 (392.50)
	Median	725.5	592.0	687.0
	Min, Max	1, 1437	1, 1411	1, 1437

	Statistic	Retacrit (N = 4496)	Silapo (N = 1841)	Total (N = 6337)
Exposure to Epoetin Zeta (in days)				
	n	4496	1841	6337
	Mean (SD)	681.3 (395.87)	626.3 (375.91)	665.3 (390.94)
	Median	725.5	592.0	687.0
	Min, Max	1, 1158	1, 1156	1, 1158

Statistic	Retacrit (N = 4496)	Silapo (N = 1841)	Total (N = 6337)
No Data Reported.			

	Retacrit (N = 4496)		Silapo (N = 1841)		Total (N = 6337)	
Duration of Treatment	n(%)	Patient-Years	n(%)	Patient-Years	n(%)	Patient-Years
Cumulative up to 6 Months	715 (15.9)	186.7	276 (15.0)	66.5	991 (15.6)	253.3
Cumulative up to 12 Months	1296 (28.8)	679.4	563 (30.6)	275.6	1859 (29.3)	955.0
Cumulative up to 18 Months	1788 (39.8)	1354.4	856 (46.5)	639.3	2644 (41.7)	1993.7
Cumulative up to 24 Months	2261 (50.3)	2235.1	1081 (58.7)	1029.4	3342 (52.7)	3264.5
Cumulative up to 30 Months	2582 (57.4)	2991.1	1248 (67.8)	1403.0	3830 (60.4)	4394.1
Cumulative up to 36 Months	3766 (83.8)	6423.2	1556 (84.5)	2279.8	5322 (84.0)	8703.0
Cumulative beyond 36 Months	4496 (100.0)	8667.2	1841 (100.0)	3170.3	6337 (100.0)	11837.6

Duration of Treatment	Retacrit (N = 4496) n(%)	Retacrit (N = 4496) Patient-Years	Silapo (N = 1841) n(%)	Silapo (N = 1841) Patient-Years	Total (N = 6337) n(%)	Total (N = 6337) Patient-Years
Cumulative up to 6 Months	715 (15.9)	186.7	276 (15.0)	66.5	991 (15.6)	253.3
Cumulative up to 12 Months	1296 (28.8)	679.4	563 (30.6)	275.6	1859 (29.3)	955.0
Cumulative up to 18 Months	1788 (39.8)	1354.4	856 (46.5)	639.3	2644 (41.7)	1993.7
Cumulative up to 24 Months	2261 (50.3)	2235.1	1081 (58.7)	1029.4	3342 (52.7)	3264.5
Cumulative up to 30 Months	2582 (57.4)	2991.1	1248 (67.8)	1403.0	3830 (60.4)	4394.1
Cumulative up to 36 Months	3766 (83.8)	6423.2	1556 (84.5)	2279.8	5322 (84.0)	8703.0
Cumulative up to and beyond 36 Months	4496 (100.0)	8661.3	1841 (100.0)	3156.9	6337 (100.0)	11818.2

	Statistic	Retacrit (N = 4496)	Silapo (N = 1841)	Total (N = 6337)
Exposure Duration from 38th Month to Last Exposure (in days)				
	n	71	73	144
	Mean (SD)	31.7 (47.87)	68.2 (55.78)	50.2 (54.99)
	Median	20.0	57.0	26.0
	Min, Max	1, 282	3, 256	1, 282