

Intravenous Iron Postauthorisation Safety Study (PASS): Evaluation of the Risk of Severe Hypersensitivity Reactions

First published: 30/11/2017

Last updated: 02/07/2024

Study

Finalised

Administrative details

EU PAS number

EUPAS20720

Study ID

42909

DARWIN EU® study

No

Study countries

 Denmark

 France

 Germany

 Netherlands

Study description

In September 2013, the European Medicines Agency Pharmacovigilance Risk Assessment Committee (EMA-PRAC) recommended that marketing authorisation holders of intravenous iron compounds conduct a postauthorisation safety study (PASS) to further characterise the safety concerns regarding hypersensitivity reactions. This is a multinational, longitudinal cohort study of new users of intravenous iron compounds conducted in populations covered through electronic health databases and patient registries in Denmark, the Netherlands, France, Germany, and Sweden. The study aims to evaluate the risk of anaphylactic or severe immediate hypersensitivity reactions on the day of or the day after the first intravenous iron use by estimating the incidence proportions of anaphylactic reactions in patients who were first dispensed/administered intravenous iron (new users). Incidence estimates will be calculated for patients overall, by group of intravenous iron product, and by type of intravenous iron product. Risk ratios will be used to compare the risk of anaphylaxis between intravenous iron groups and among the various intravenous iron types at the first exposure. The risk of anaphylactic reactions among new users of an intravenous anaphylaxis marker (penicillin), a compound for which anaphylaxis is a well-recognised side effect, will be estimated to provide context for the risk in users of intravenous iron.

Study status

Finalised

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)



France



Spain



Sweden



United Kingdom



United Kingdom (Northern Ireland)



United States

First published: 21/04/2010

Last updated: 11/08/2026

Institution

Not-for-profit

ENCEPP partner

Innovation Monitoring and Health Technology Assessment, German Institute for Medical Documentation and Information (DIMDI)



Germany

First published: 05/11/2010

Last updated: 20/08/2024

Institution

Other

Leibniz Institute for Prevention Research and Epidemiology - BIPS



Germany

First published: 29/03/2010

Last updated: 30/03/2026

Institution

Not-for-profit

ENCePP partner

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

 Denmark

First published: 20/07/2021

Last updated: 08/05/2026

Institution

Educational Institution

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

 Netherlands

First published: 07/01/2022

Last updated: 19/12/2025

Institution

Non-Pharmaceutical company

ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

 Sweden

First published: 24/03/2010

Last updated: 02/06/2026

Institution

Educational Institution

Laboratory/Research/Testing facility

Not-for-profit

ENCEPP partner

RTI Health Solutions (RTI-HS)

 France

 Spain

 Sweden

 United Kingdom

 United Kingdom (Northern Ireland)

 United States

First published: 21/04/2010

Last updated: 11/08/2026

Institution

Not-for-profit

ENCEPP partner

Bordeaux PharmacoS, University of Bordeaux

 France

First published: 07/02/2023

Last updated: 08/12/2025

Institution

Educational Institution

Hospital/Clinic/Other health care facility

Not-for-profit

ENCePP partner

Carl von Ossietzky University of Oldenburg
Oldenburg, Germany, University Hospital of
Cologne - Board of Trustees for Dialysis and
Kidney Transplantation (KfH-QiN) Cologne,
Germany

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Lia Gutierrez

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/02/2017

Actual: 16/03/2017

Study start date

Planned: 30/03/2018

Actual: 09/03/2018

Date of final study report

Planned: 30/03/2020

Actual: 29/04/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

IV Iron Marketing Authorisation Holders (MAH) Consortium, comprising 17 MAHs
(see Annex 3 in protocol for full list)

Study protocol

[IV_Iron_PASS_AmendedProtocol_v1.1_04May2017_Redacted.pdf](#) (2.31 MB)

[IVfePASS_Protocol_V2.1_FINAL_26September2019_Redacted_ok.pdf](#) (4 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 1 (imposed as condition of marketing authorisation)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To assess the risk of anaphylactic or severe immediate hypersensitivity reactions on the day of or the day after the first intravenous iron use among patients with various indications for intravenous iron, overall and by groups and

types, and to compare the risk between intravenous iron groups (i.e. dextrans vs. non-dextrans) and among the various intravenous iron types.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Postauthorisation Safety Study (PASS)

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B03AC) Iron, parenteral preparations

Iron, parenteral preparations

Medical condition to be studied

Anaphylactic reaction

Population studied

Short description of the study population

The study cohort comprised all adults from the source population who had a first recorded dispensing/administration of IV iron during the study period, were continuously enrolled or registered in the data source for at least 12 months

before the first recorded iron treatment and were at least 18 years of age on the date of the first dispensing/administration of IV iron. Second or subsequent dispensing/administration of the same type of IV iron meeting the inclusion criteria were also considered for the corresponding analyses. For the KfH QiN dialysis registry in Germany, the eligibility requirement for a minimum continuous enrolment of 12 months before the first IV iron administration was not applied because medical information is captured only from the date patients' initiate dialysis. The same selection criteria were applied to the IV penicillins cohort in the data sources where IV penicillins use was captured (i.e., Danish national and regional linked registries and databases, PHARMO-NL, SNDS in France, and GePaRD in Germany).

Age groups

- Adults (18 to < 46 years)
 - Adults (46 to < 65 years)
 - Adults (65 to < 75 years)
 - Adults (75 to < 85 years)
 - Adults (85 years and over)
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Special population of interest

Renal impaired

Estimated number of subjects

250000

Study design details

Outcomes

Anaphylactic reactions or severe immediate hypersensitivity reactions.

Data analysis plan

Descriptive statistics will be calculated to summarise baseline characteristics at cohort entry by groups and specific intravenous iron types and for the cohorts of intravenous penicillin. Propensity scores will be estimated by using multivariable logistic regression, with the dependent variable 1 for the primary intravenous iron group (or type) of interest or 0 for the comparator intravenous iron group (or type) and all of the prespecified covariates included as independent variables. If numbers are adequate, incidence proportions and risk ratios will be estimated individually in each data source by intravenous iron group and for each intravenous iron type, using iron sucrose as the common comparator group. Analyses will be conducted in each data source separately, and pooled estimates will be calculated if deemed appropriate.

Documents

Study results

[IV Iron PASS_Abstract_results_Redacted.pdf](#) (62.88 KB)

[IV Iron PASS_Final Report_Revised V1.3_20Nov2020_Redacted.pdf](#) (6.9 MB)

Study, other information

[Annex5_DoIForm_EUPASnumber_Update11Feb2020.pdf](#) (1.52 MB)

[Annex5_DOI_SAB_ABircher.pdf](#) (2.45 MB)

[IV Iron_DoIForms_2_2.pdf](#) (2.27 MB)

[IV Iron_DoIForms_2_2_update_5Feb2019.pdf](#) (2.22 MB)

[IV Iron_DoIForms_3_3.pdf](#) (198.54 KB)

[IV-IRON_DOI CDP-20190207.pdf](#) (1.48 MB)

[NewDoI_updated_5Feb2019.pdf](#) (966.42 KB)

Study publications

[Fortuny J, von Gersdorff G, Lassalle R, Linder M, Overbeek J, Reinold J, Toft G...](#)

[de Sordi D, Kappen S, Otto-Sobotka F, Kulschewski A, Weyland A, Gutierrez L, Fo...](#)

[Gutierrez L, Bezemer ID, Dress J, Ehrenstein V, Forstner M, Franzoni C, Lassall...](#)

[Gutierrez L, Blin P, Dress J, Droz-Perroteau C, Ehrenstein V, Franzoni C, Kollh...](#)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

[IV Iron_DoIForms_1_2.pdf](#) (2.97 MB)

[IV Iron_DoIForms_1_2_update_5Feb2019.pdf](#) (2.67 MB)

Composition of steering group and observers

[IV Iron Steering Committee.pdf](#) (74.47 KB)

[Steering Committee List_2019.pdf](#) (95.54 KB)

Signed code of conduct

[2017-0046_Declaration_EUPAS20720.pdf](#) (97.3 KB)

Signed code of conduct checklist

[2017-0046_Checklist_EUPAS20720.pdf](#) (459.83 KB)

Signed checklist for study protocols

[2017-0046_Checklist for Study Protocols_EUPAS20720.pdf](#) (85.1 KB)

Data sources

Data source(s)

Danish registries (access/analysis)

PHARMO Data Network

German Pharmacoepidemiological Research Database

Data sources (types)

[Administrative healthcare records \(e.g., claims\)](#)

[Disease registry](#)

[Drug dispensing/prescription data](#)

[Electronic healthcare records \(EHR\)](#)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No