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	FRANCE		PRIVACY		61 Years	Male	Unk	03	AUG	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Hypertriglyceridemia [Hypertriglyceridaemia]
RENAL FAILURE [Renal failure]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL). This is a Non-Interventional Study report with non-serious events 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) Bosulif (BOSUTINIB) Film-coated tablet
#2) EXFORGE (AMLODIPINE BESILATE, VALSARTAN)
(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) 400 mg, 1x/day	#1) Unknown
#2)	#2) Unknown

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) 16-DEC-2015 / 25-APR-2019	#1) 3 years 4 months 10 days
#2) 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
1999 to Ongoing	Relevant Med History	Inflammatory rheumatism (Rheumatic disorder)
JUN-2014 to Ongoing	Relevant Med History	Pleural effusion (Pleural effusion)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021104819

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
01-FEB-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021104819

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 61-year-old male subject received bosutinib (BOSULIF) from 16Dec2015 to 25Apr2019 at 400 mg once daily and from 26Apr2019 at 300 mg once daily and amlodipine besilate / valsartan (EXFORGE) from an unknown date at unknown dose, both for an unknown indication.
Medical history included ongoing Inflammatory rheumatism from 1999, ongoing pleural effusion from Jun2014 and myocardial infarction in Nov2015.
Concomitant medications, if any, were not reported.
On 03Aug2018, the subject experienced hypertriglyceridemia, rated as grade 1. In response to this event, no action was taken with bosutinib.
On 11Apr2019, the subject experienced renal failure, rated as grade 1. In response to this event, the dose of bosutinib was reduced and amlodipine besilate / valsartan (EXFORGE) was discontinued. At the time of the report, the subject had not recovered from the event renal failure. The clinical outcome of the event hypertriglyceridemia was unknown.

According to the reporter, renal failure was not related to study drug but related to concomitant medication amlodipine besilate / valsartan. According to the investigator, the event hypertriglyceridemia was related to bosutinib but not related to concomitant medications.

Case Comment: The limited information provided precludes a full clinical assessment of the case. Significant in the assessment of causality would be concomitant medications, diagnosis, stage and extent of the underlying malignancy, and possible confounding factors like dietary habit and level of hydration, which were unknown at the time of the report. Based on available information and until further data is provided, the Company deems there is not a reasonable possibility that hypertriglyceridemia and renal failure are related to bosutinib regimen ongoing from more than five years.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-APR-2019	Blood creatinine	171 umol/l	104 59
2	03-AUG-2018	Blood triglycerides	2.49 mmol/L	1.7 0.4

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, 1x/day; Unknown	Unknown	26-APR-2019 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
NOV-2015 to NOV-2015	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
PRIVACY	FRANCE		PRIVACY		72 Years	Male	90.00 kg	24	NOV	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Dyspnea [Dyspnoea]

Case Description: The initial case was missing the following minimum criteria: non-fatal disease progression is not reportable for anti-cancer product in clinical study. Upon receipt of follow-up information on 28Feb2023, this case now contains all required information to be considered valid.

OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 28-JAN-2020 / 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) JANUMET (METFORMIN HYDROCHLORIDE, SITAGLIPTIN PHOSP
#2) DIPROSONE [BETAMETHASONE SODIUM PHOSPHATE] (BETAMETH
#3) LAMISIL [TERBINAFINE] (TERBINAFINE) ; JUL-2019 / Ongoing
#4) ARKOLEVURE (INULIN, SACCHAROMYCES BOULARDII) ; SEP-2019 / 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
2007 to Ongoing	Relevant Med History	Diabetes (Diabetes mellitus)
Unknown to Ongoing	Relevant Med History	Psoriasis (Psoriasis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021129742

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-FEB-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report received from a contactable reporter(s) (Physician) for protocol B1871047.

A 72-year-old male patient received bosutinib (BOSULIF), since 28Jan2020 at 500 mg daily. The patient's relevant medical history included: "Diabetes", start date: 2007 (ongoing); "Psoriasis" (ongoing); "Chronic sinusitis" (ongoing); "Mycosis", start date: Jul2019 (unspecified if ongoing). Concomitant medication(s) included: JANUMET oral taken for diabetes mellitus, start date: 2007 (ongoing); DIPROSONE [BETAMETHASONE SODIUM PHOSPHATE] taken for psoriasis (ongoing); LAMISIL [TERBINAFINE] oral taken for fungal infection, start date: Jul2019 (ongoing); ARKOLEVURE oral taken for constipation, start date: Sep2019 (ongoing).
The following information was reported: DYSPNOEA (non-serious) with onset 24Nov2020, outcome "not recovered", described as "Dyspnea". The action taken for bosutinib was dosage not changed.
Additional information: The event of dyspnea was rated grade 1, the action taken for bosutinib in response to the event dyspnea was reported as dose not changed. The dyspnea event was still in progress at the end of the study. It was also reported an additional event of "loss of response" with onset 30Dec2019, reported as non-serious rated grade 2, for which the action taken for bosutinib was dosage increased, the event resulted as resolved on 02Jun2020, according to the reporter, the event was related to bosutinib and unrelated to concomitant drugs.

The reporter considered "dyspnea" related to bosutinib and unrelated to concomitant drugs

Follow-up attempts are completed. No further information is expected

Case Comment: The Company considers the reported event "dyspnea" is related to bosutinib and unrelated. This case will be reassessed should additional information become available.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#1) JANUMET (METFORMIN HYDROCHLORIDE, SITAGLIPTIN PHOSPHATE MONOHYDRATE) ; 2007 / Ongoing

#2) DIPROSONE [BETAMETHASONE SODIUM PHOSPHATE] (BETAMETHASONE SODIUM PHOSPHATE) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Chronic sinusitis (Chronic sinusitis);
JUL-2019 to Unknown	Relevant Med History	Mycosis (Fungal infection);

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	FRANCE		PRIVACY		24 Years	Female	58.00 kg	30	SEP	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

IRON DEFICIENCY [Iron deficiency]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 14-NOV-2018 / 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
MAY-2009 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021152516

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
24-APR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 25-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since 14Nov2018 (ongoing) at 300 mg 1x/day. The patient's relevant medical history included: "CHRONIC MYELOID LEUKEMIA", start date: May2009 (ongoing). The patient's concomitant medications were not reported. The following information was reported: IRON DEFICIENCY (non-serious) with onset 30Sep2020, outcome "not recovered". The event iron deficiency (abundant and painful periods) was rated grade 2. Treatment included ferritin dosage on 30Sep2020 was 28 ng/ml and ascorbic acid/ ferrous sulfate (TIMOFEROL). The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of iron deficiency.

The event was not related to bosutinib or to any concomitant drug.

No follow-up attempts are possible. No further information is expected.

Follow-up (10May2022): This is a non-interventional study follow-up report for protocol B1871047. Updated information: outcome of the event iron deficiency was updated to not resolved. Recovery date deleted.

No follow-up attempts are possible. No further information is expected.

Follow-up (24Apr2023): This is a non-interventional study follow-up report from the CRO for protocol B1871047.
Updated information included: updated patient's DOB, event description.

Case Comment: In concurrence with the reporter, the Company deems the reported Iron deficiency (abundant menstruation) unrelated to bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-SEP-2020	Serum ferritin	28 ng/ml	

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	FRANCE		PRIVACY		59 Years	Female	118.00 kg			2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

gingivitis [Gingivitis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) SPIRAMYCINE (SPIRAMYCINE)
(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) 200 mg, daily	#1) Unknown
#2) UNK	#2) Unknown

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) 25-SEP-2018 / 07-DEC-2020	#1) 2 years 2 months 13 days
#2) 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
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021152549

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old female patient received bosutinib (BOSULIF), first regimen from 25Sep2018 to 07Dec2020 at 200 mg daily and second regimen since 08Dec2020 (ongoing) at 300 mg daily; spiramycine (SPIRAMYCINE), (Batch/Lot number: unknown); metronidazole (METRONIDAZOLE), (Batch/Lot number: unknown). The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: GINGIVITIS (non-serious) with onset 2020, outcome "recovered" (08Dec2020). The event was rated grade 1. The action taken for bosutinib was dosage not changed. The action taken for spiramycine and metronidazole was dosage permanently withdrawn.

The investigator considered that the event was unrelated to bosutinib and related to concomitant drugs spiramycin and metronidazole.

Follow-up (24Jul2023): This is a follow-up report from a Non-Interventional Study source for Protocol B1871047 received from the CRO. Updated information included: Bosulif details.

Follow-up (28Jul2023): This is a follow-up report from a Non-Interventional Study source for Protocol B1871047 received from the CRO. Updated information included: Bosulif details (new dosage regimens).

Follow-up (27Sep2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: Bosutinib was taken at 200 mg daily from 25Sep2018 to 07Dec2020 then at 300 mg daily from 08Dec2020 and ongoing. Medical history included ongoing chronic myeloid leukemia. In response to the gingivitis, spiramycin and metronidazole were discontinued.

Follow-up (25Oct2023): This is a non-interventional study follow-up report received from clinical team. Updated information included: action taken updated to dose not changed.

Case Comment: In concurrence with the reporting investigator, the Company deems the reported gingivitis unrelated to bosutinib administration. The follow-up information received does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	Unknown	08-DEC-2020 / Ongoing; Unknown
#3) METRONIDAZOLE (METRONIDAZOLE) ; Regimen #1	UNK; Unknown	Unknown	Unknown; 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
PRIVACY	FRANCE		PRIVACY		55 Years	Female	85.00 kg		JAN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Increased hypoxia [Hypoxia]
Urinary infection [Urinary tract infection]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL). This is a Non-Interventional Study report with non-serious events 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) Bosutinib (BOSUTINIB) Unknown

(Continued on Additional Information Page)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 300 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 12-APR-2017 / 25-JUL-2018	#1) 1 year 3 months 14 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	Past Drug Event	
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021152651

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 55-year-old female patient (unknown if pregnant) received bosutinib (BOSUTINIB), first regimen from 12Apr2017 to 25Jul2018 at 300 mg daily and second regimen since 26Jul2018 (ongoing) at 400 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing); "arterial hypertension" (ongoing). The patient's concomitant medications were not reported. Past drug history included: Dasatinib, reaction(s): "Pulmonary hypertension".
The following information was reported: HYPOXIA (non-serious) with onset Jan2020, outcome "unknown", described as "Increased hypoxia"; URINARY TRACT INFECTION (non-serious), outcome "unknown", described as "Urinary infection". Therapeutic measures were taken as a result of urinary tract infection.

The clinical course was reported as follows: The subject was hospitalized from 13Jan2020 to 14Jan2020 for a reassessment of a pulmonary arterial hypertension reported when taking dasatinib therefore before the study. This hospitalization should not be declared because there was no worsening of this pathology but increased hypoxia was noted during this hospitalization and should be controlled. The Urinary infection was treated with cefixime from Nov2020 to Nov2020. The subject did not have aggravation of her pulmonary state. She was very regularly medically followed in pneumology service unit and the short hospitalization in Jan2020 was scheduled to reassess her disease. No aggravation was noticed. The subject was seen on 24Aug2020 without any concern and no modification of the medical cares. The action taken with bosutinib in response to the events, clinical outcome and causality assessment was not provided. The investigator had not confirmed these events with the subject. As of 10Oct2023, it was reported the event urinary infection was non-serious and rated grade 1, outcome unknown, unrelated to bosutinib, action taken was not applicable. Onset date was deleted. The event Increased hypoxia was non-serious and rated grade 1, outcome unknown, unrelated to bosutinib, action taken was not applicable.

The reporter considered "increased hypoxia" and "urinary infection" not related to bosutinib.

Follow-up (09Apr2021): New information received from contactable physician includes: event details.

Follow-up (11Mar2023): This is a non-interventional study follow-up report received from the investigational site via CRO.
Updated information included: patient data (age, gender, height, weight), reaction data (verbatim for event "urinary tract infection" updated to "Urinary infection").

Follow-up (10Oct2023): new information received from CRO is as follows: Medical history (chronic myeloid leukemia, arterial hypertension); for BOSULIF: dosage regimen added, Action taken updated as Not applicable; For events urinary infection and Increased hypoxia: Onset date removed, Reporter causality added (unrelated).

Case Comment: Based on available information, a possible contributory role of the subject drug BOSUTINIB cannot be excluded for the reported events Increased hypoxia and Urinary tract infection. Medical history of pulmonary hypertension may provide an alternative cause for hypoxia.

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) Bosutinib (BOSUTINIB) Unknown; Regimen #2	400 mg, daily; Unknown	Unknown	26-JUL-2018 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event	DASATINIB (DASATINIB); Drug Reaction: Pulmonary hypertension (Pulmonary hypertension)
Unknown to Ongoing	Relevant Med History	Arterial 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	FRANCE		PRIVACY		23 Years	Female	58.00 kg		NOV	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

DIARRHEA [Diarrhoea]
CYSTITIS [Cystitis]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, 1x/day	#1) Unknown

17. INDICATION(S) FOR USE
#1) CHRONIC MYELOID LEUKEMIA (Chronic myeloid leukaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 14-NOV-2018 / 20-NOV-2018	#1) 7 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
MAY-2009 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)
2009 to 2009	Relevant Med History	Splenomegaly (Splenomegaly)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021153403

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
15-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 23-year-old female subject started to receive bosutinib (BOSULIF) at 200 mg 1x/day from 14Nov2018 to 20Nov2018, at 300 mg 1x/day from 21Nov2018 to 27Nov2018, at 400 mg 1x/day from 28Nov2018 to 13Feb2019 and ongoing at 300 mg 1x/day from 14Feb2019 for chronic myeloid leukaemia. Relevant medical history included chronic myeloid leukaemia since May2009 and splenomegaly in 2009. Relevant concomitant medication, if any, was not provided. In Nov2018 the subject experienced diarrhea in the afternoon of taking bosutinib. In Feb2019 she experienced cystitis. Treated with Spasn from 13Feb2019 and with Tiorfan from 19Jan2021 she received antibiotic for repeat cystitis (Amoxicillin, Augmentin and Cefixime). It was reported that at the time of initial declaration with aggravation affecting quality of life. Due to diarrhea bosutinib dose was reduced while no action was taken in response to the event cystitis. The outcome of the event diarrhea was recovering while cystitis recovered on 03Jun2019.

The event diarrhea was rated with grade 2, reported as non serious, related to BOSULIF and unrelated to concomitant medication. The event cystitis was rated with grade 2, reported as non serious, unrelated to BOSULIF and unrelated to concomitant medication.

Follow-up (10May2022): This is a non-interventional study follow-up report received from a contactable reporter(s) (Physician) for protocol B1871047.

Updated information: event term "digestive disorders/diarrhea" was updated to "diarrhea".

No follow-up attempt initiated. No further information expected.

Follow-up (15Sep2023): This is a non-interventional study follow-up report received from the investigational site via the CRO. Updated information includes: bosutinib daily dose, onset date and outcome of the event diarrhea.

Case Comment: Based on the information currently available, a possible contributory role of bosutinib to the reported event Diarrhoea cannot be completely excluded based on temporal association. There was not a reasonable possibility that the event Cystitis was related to bosutinib, but most likely represents patient intercurrent medical condition.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, 1x/day; Unknown	CHRONIC MYELOID LEUKEMIA (Chronic myeloid leukaemia)	21-NOV-2018 / 27-NOV-2018; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg, 1x/day; Unknown	CHRONIC MYELOID LEUKEMIA (Chronic myeloid leukaemia)	28-NOV-2018 / 13-FEB-2019; 2 months 17 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	300 mg, 1x/day; Unknown	CHRONIC MYELOID LEUKEMIA (Chronic myeloid leukaemia)	14-FEB-2019 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		25 Years	Female	58.00 kg		DEC	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

HAIR LOSS TENDENCY [Alopecia]
FLU SYNDROME [Influenza]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047, Study alias BOSEVAL. This is a non-interventional clinical study case reporting non-serious events 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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 14-NOV-2018 / 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
MAY-2009 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)
2009 to 2009	Relevant Med History	Splenomegaly (Splenomegaly)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021153428

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-MAY-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 25-years-old female subject started to receive bosutinib (BOSULIF), via an unspecified route of administration from 14Nov2018 and ongoing at 300 mg, 1x/day for an unspecified indication. Medical history included chronic myeloid leukaemia from May2009 and ongoing, splenomegaly in 2009. The patient's concomitant medications were not reported. The subject experienced hair loss tendency on Dec2019 with outcome of recovered on 30Sep2020, flu syndrome on 17Mar2020 with outcome of recovered. The event tendency hair loss was rated grade 1 and not serious. The event flu syndrome was rated grade 1 and not serious. The event flu syndrome was described as hyperthermia + asthenia + anosmia + agueusia evokative of a COVID infection. Serology test COVID was negative on 30Sep2020. The action taken in response to the events for bosutinib was dose not changed.

The investigator assessed the event hair loss tendency as unrelated to bosutinib and the event flu syndrome as unrelated to study drug bosutinib.

Follow-up (10May2022) : This is a follow-up to a non-interventional study for protocol B1871047.

Updated information : onset date of the event hair loss tendency was corrected to Dec2019, causality assessment for the event hair loss tendency was corrected to unrelated to bosutinib, event "flu syndrome (suspicion COVID)" was corrected to "flu syndrome".

No follow-up attempt initiated. No further information expected.

Case Comment: In concurrence with the investigator, the Company considers the reported events hair loss tendency and the event flu syndrome (suspicion COVID) as unrelated to the suspect drug bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	30-SEP-2020	SARS-CoV-2 antibody test Negative	negative	

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	FRANCE		PRIVACY		62 Years	Male	Unk	20	JAN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

COPD DECOMPENSATION [Chronic obstructive pulmonary disease]
Painful tendons [Tendon pain]
Painful tendons cramps [Muscle spasms]
rhinopharyngitis [Nasopharyngitis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) Atorvastatin Calcium (ATORVASTATIN CALCIUM) Unknown
(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) 400 mg, 1x/day	#1) Unknown
#2) 80 mg, daily	#2) Oral

17. INDICATION(S) FOR USE
#1) Unknown
#2) DYSLIPIDEMIA (Dyslipidaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 03-APR-2019 / 30-MAY-2019	#1) 1 month 28 days
#2) 2019 / 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
Unknown to Ongoing	Relevant Med History	CML (Chronic myeloid leukaemia)
Unknown to Ongoing	Relevant Med History	COPD (Chronic obstructive pulmonary disease)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021161629

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

A 62-year-old male patient started to receive bosutinib (BOSULIF) via an unspecified route of administration from 03Apr2019 to 30May2019 at 400 mg, once daily (1x/day), via an unspecified route of administration from an unspecified date and ongoing at 300 mg, once daily (1x/day) for an unspecified indication, atorvastatin calcium oral from 2019 to an unspecified date at 80 mg daily, via an unspecified route of administration from 09Feb2021 to an unspecified date at 40 mg, daily for dyslipidaemia. Medical history included ongoing chronic myeloid leukaemia (CML), ongoing chronic obstructive pulmonary disease (COPD), ongoing dyslipidaemia, ongoing arteriopathy. The patient's concomitant medications were not reported.
The patient experienced COPD decompensation on 24Jan2020, which rated grade 3, patient was hospitalized from 27Jan2020 to 30Jan2020 for COPD decompensation. On 20Jan2020, patient had rhinopharyngitis, non-serious grade 2. Consultation with the attending physician on 23Jan2020 with prescription of prednisone and amoxicillin/ clavulanate potassium (AUGMENTIN). Normal biological tests. On 25Jan2020, disappearance of nasopharyngeal symptoms but appearance of inspiratory breathlessness different from COPD. Patient must sleep sitting because feeling of suffocation when lying down. He was limited in his daily activities. In addition, there was a wet cough, no fever. Emergency visit on 27Jan2020 for acute dyspnea on COPD (neurologic examination: mild trembling of the left hand at the bar. no sign of focus, no meningeal sign, no sensory-motor deficit). Conclusion: decompensation of COPD, following a rhinopharyngitis, no pulmonary infectious focus. The patent also experienced painful tendons cramps on unknown date in 2020, non-serious, rated grade 1. Cramps with tendinous pain were possibly related to statins with reduced dose of atorvastatin (80 to 40mg / day) on 09Feb2021. The action taken in response to the events for bosutinib was dose not changed. Drug atorvastatin calcium was dose reduced due to painful tendons cramps. The outcome of event COPD decompensation was recovered on 30Jan2020, of event painful tendons cramps was recovered on 10Aug2021, of event rhinopharyngitis was resolved on 25Jan2020.

The investigator considered that the events COPD decompensation and rhinopharyngitis were unrelated to bosutinib or to any concomitant drug and that Painful tendons cramps was unrelated to bosutinib and related to concomitant drug atorvastatin.

Follow-up (10May2022): This is a follow-up report to notify that the cases AER 2021161629 and AER 2021192869 are duplicates. All subsequent follow-up information will be reported under manufacturer report number AER 2021161629. The new information reported from a contactable reporter(s) (Physician) includes: events details (COPD decompensation was rated grade 3 and occurred on 24Jan2020. The events painful tendons cramps was split for Cramps and Painful tendons and resolved on 10Aug2021, New event rhinopharyngitis).

Follow-up (27Oct2023): This follow-up report is being submitted to amend previously transmitted information: onset date of event COPD decompensation updated.

Case Comment: The Company concurs with the investigator that there is no sufficient evidence to conclude a causal role of study drug bosutinib to reported "decompensation of COPD", "rhinopharyngitis", and "painful tendons cramps". "Decompensation of COPD" and "rhinopharyngitis" are also considered unrelated to atorvastatin calcium, and are more likely associated with subject's ongoing medical conditions (including ongoing medical history of COPD). Based on available information and known safety profile of atorvastatin calcium, the reasonable possibility of an association between atorvastatin calcium and "painful tendons cramps" cannot be ruled out.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Body temperature	no fever	
2	23-JAN-2020	Laboratory test	normal	
3	27-JAN-2020	Neurological examination no sign of focus, no meningeal sign, no sensory-motor deficit	mild trembling of the left hand at the bar	

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) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, 1x/day; Unknown	Unknown	Ongoing;

Mfr. Control Number: 2021161629

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
Regimen #2			Unknown
#2) Atorvastatin Calcium (ATORVASTATIN CALCIUM) Unknown; Regimen #2	40 mg, daily; Unknown	DYSLIPIDEMIA (Dyslipidaemia)	09-FEB-2021 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Dyslipidemia (Dyslipidaemia);
Unknown to Ongoing	Relevant Med History	Arteriopathy (Arterial 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
PRIVACY	FRANCE		PRIVACY		71 Years	Male	84.00 kg	29	MAR	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Slow increase of atheromatous lesions of lower limbs [Arteriosclerosis]
Slow increase of atheromatous lesions of lower limbs [Condition aggravated]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol

(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) Bosulif (BOSUTINIB) Film-coated tablet
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☒ NO ☐ NA

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

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) 31-MAY-2016 / 12-JUN-2019

19. THERAPY DURATION
#1) 3 years 13 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
2013 to Ongoing	Relevant Med History	Cardiomyopathy (Cardiomyopathy)
2000 to Ongoing	Relevant Med History	Diabetes (Diabetes mellitus)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021166309

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
12-JUN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021166309

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

B1871047.

A 71-year-old male patient received bosutinib (BOSULIF), first regimen from 31May2016 to 12Jun2019 at 300 mg 1x/day and second regimen since 13Jun2019 at 200 mg 1x/day. The patient's relevant medical history included: "Cardiopathy", start date: 2013 (ongoing); "Diabetes", start date: 2000 (ongoing); "Pancreas cancer", start date: 04Aug2015 (ongoing); "Hypertension arterial", start date: 1986 (ongoing); "asthma" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: ARTERIOSCLEROSIS (non-serious), CONDITION AGGRAVATED (non-serious) all with onset 29Mar2018, outcome "not recovered" and all described as "Slow increase of atheromatous lesions of lower limbs". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage reduced.
The reporter considered "slow increase of atheromatous lesions of lower limbs" related to bosutinib.

Additional information: The event was grade 2. This was also observed on ultrasound doppler in the beginning of Jun2019. As atheromatous lesions were present before the patient was enrolled to the study there was little probability that this increase was due to bosutinib. However this led to decrease of dose to 200 mg a day from 13Jun2019. At day of consultation on 12Jun2019 subject was also dyspneic with decrease of walking perimeter. Comment per reporter: The subject experienced dyspnea of effort on 23Apr2018, probably linked to her heart failure and therefore not be considered an adverse event. In the medical file, it is noted "the subject describes chronic dyspnea for minor efforts". The subject also has active asthma and the physician notes that the dyspnea may be of multifactorial origin. Heart failure and asthma are well declared in the history, which is why dyspnea was not considered as an adverse event. The investigator confirmed that the dyspnea was a symptom of subject's cardiac pathology and it not to be reported as additional SAE. According to the investigator event was related to study drug.

Follow-up (16Nov2021): new information received from the investigator via the CRO included updated onset date, grading and causality of the event.

Follow-up (10May2022): This is a follow-up Non-Interventional Study report (Post Authorization Safety Study) for protocol B1871047 from a contactable physician.
Updated information: the investigator confirmed that the dyspnea was a symptom of subject's cardiac pathology and it not to be reported as additional SAE and Medical history (asthma) added.

Amendment: This follow-up report is being submitted to amend previously reported information: last follow-up received date was corrected (updated to 10May2022) in the narrative; updated patient's age.

Case Comment: The Company, according to medical history suggesting that atheromatous lesions is a pre-existing medical condition deems there is not a reasonable possibility that the reported slow increase of atheromatous lesions of lower limbs is related to the study drug, bosutinib. 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	JUN-2019	Ultrasound Doppler	slow increase of atheromatous lesions of lower lim	

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, 1x/day; Unknown	Unknown	13-JUN-2019 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
04-AUG-2015 to Ongoing	Relevant Med History	Pancreas cancer (Pancreatic carcinoma);
1986 to Ongoing	Relevant Med History	Hypertension arterial (Hypertension);
Unknown to Ongoing	Relevant Med History	Asthma (Asthma);

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	FRANCE		PRIVACY		53 Years	Female	Unk		MAY	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

dental abscess [Tooth abscess]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. This is a Non-Interventional Study report with non-serious event 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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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	Relevant Med History	None ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021177902

24c. DATE RECEIVED BY MANUFACTURER
30-MAY-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 53-year-old subject started to receive bosutinib (BOSULIF), via an unspecified route of administration from an unspecified date to an unspecified date at an unspecified dose for an unspecified indication. Medical history was none. The patient's concomitant medications were not reported. The subject experienced dental abscess in May2020. The event was reported as non-serious and rated grade 1. Corrective treatment included azithromycin. The action taken in response to the event for bosutinib was not applicable. The outcome of event was resolved in 02Jun2020.

According to the investigator, the event was not related to study drug or concomitant medication.

Follow-up (07Apr2021):New information reported from the site includes: event downgraded to non-serious, rated grade 1 and action taken with bosutinib updated from "Unknown" to "Dose not changed".

Follow-up (30May2023) This is a non-interventional study follow up report received from the investigational site via CRO. Updated information includes: action taken (updated to not applicable) and event details (onset date and stop date updated).

Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the information currently available, pending more details regarding the clinical course of the reported dental abscess, at this moment, in concurrence with the reporter, the Company deems the reported event an intercurrent disease, unrelated to the administration of bosutinib.

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	FRANCE		PRIVACY		46 Years	Female	59.50 kg		MAR	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

emotional eczema [Eczema]
cough without fever [Cough]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 400 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) chronic myeloid leukemia (Chronic myeloid leukaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 24-FEB-2020 / 12-MAR-2020	#1) 18 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	Relevant Med History	Depression (Depression)
Unknown to Ongoing	Relevant Med History	CML (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021178350

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021178350

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 46-year-old female patient received bosutinib (BOSULIF), first regimen from 24Feb2020 to 12Mar2020 at 400 mg daily, second regimen from 13Mar2020 to 18Mar2020 at 500 mg daily, third regimen from 19Mar2020 to Mar2020 at 400 mg daily and fourth regimen since Mar2020 (ongoing) at 500 mg daily for chronic myeloid leukaemia. Medical history included depression and ongoing chronic myeloid leukaemia (CML). The subject was aware that depression could interact with the pain felt. Concomitant medications were not reported. The subject experienced emotional eczema and cough without fever on Mar2020. Both events emotional eczema and cough without fever were reported as non-serious (grade 1). The subject also presented with trunk rash, diarrhea and cough without fever. The diarrhea was already declared and not resolved AE (AER 2019185788) and the skin rash corresponds to eczema. The subject performed a SARS-COV-2 PCR which was negative. The subject received anti-biotherapy with amoxicillin. The action taken in response to the events for bosutinib was dose not changed. The outcome of event emotional eczema was recovered on 01Dec2020, of event cough without fever was recovered in Mar2020. According to the investigator, the both events were unrelated to bosutinib and to concomitant drugs.

Follow-up (08Jun2021): New information received from the investigator via CRO included: The outcome of the event emotional eczema was resolved on 01Dec2020 (instead of "not resolved" as previously mentioned).
No follow-up attempts are needed. No further information is expected.

Follow-up (12Jul2023): This is a follow-up to a non-interventional study for protocol B1871047 received from investigator site via the CRO. Updated information: No action was taken on bosutinib in response to event emotional eczema and cough without fever.
No follow-up attempts are needed. No further information is expected.

Follow-up (28Jul2023): This is a follow-up report received from the CRO. Updated information included: Weight updated, Relevant medical history updated with CML.

Follow-up (28Sep2023): This is a follow-up to a non-interventional study received from the investigational site via the CRO. Updated information includes: additional dosage regimen (overall start date).

Case Comment: In concurrence of the reporting investigator, the Company deems the reported emotional eczema and cough are unlikely related to the suspect, bosutinib.
The follow up information does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		SARS-CoV-2 test Negative	Negative	

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	500 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	13-MAR-2020 / 18-MAR-2020; 6 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	19-MAR-2020 / MAR-2020; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	500 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	MAR-2020 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		47 Years	Female	59.50 kg		NOV	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ASTHENIA [Asthenia]
Morose mood [Morose]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) MAR-2020 / 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	Relevant Med History	Depression (Depression)
Unknown to Ongoing	Relevant Med History	CML (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021183655

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 47-year-old female subject received bosutinib (BOSULIF), since Mar2020 (ongoing) at 500 mg daily. The subject's relevant medical history included: "Depression" (unspecified if ongoing); "CML" (ongoing). The subject's concomitant medications were not reported. The subject had been stopped from work for a week due to asthenia, with morose mood in Nov2020. The investigator clarified the known history of depression was not necessarily related to the event of morose mood (it can happen to have a morose mood without being in a depressive episode). The action taken in response to the events for bosutinib was dose not changed. The outcome of events asthenia and morose mood was resolved on 22Feb2021.

The events asthenia and morose mood were rated with grade 1, reported as non-serious, unrelated to bosutinib and unrelated to concomitant medication.

Follow-up (08Jun2021) : New information received from the investigational site via the CRO included reaction date (the event morose mood updated).

Follow-up (20Dec2021): This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047.
Updated information included: Event morose mood was updated with depression.

No follow-up attempt initiated. no further information expected.

Follow-up (21Apr2022): This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047.

Updated information includes: event depression changed to morose mood.

No follow-up attempt initiated. no further information expected.

Follow-up (30May2023): new information received from the investigator via the CRO.
Updated information included: Event Asthenia: stop date added (22Feb2021), outcome updated to recovered.

Follow-up (28July2023): new information received from the investigator via the CRO. Updated information included: Relevant medical history updated with CML

Follow-ups (28Sep2023): These are follow-ups of non-interventional study report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047; received via CRO/clinical team. Updated information included: Bosutinib dosing therapy dates (from Mar2020 ongoing).

Case Comment: The events asthenia and morose mood were reported as non-serious, unrelated to bosutinib (BOSULIF) and unrelated to concomitant medication. 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
PRIVACY	FRANCE		PRIVACY		54 Years	Male	91.00 kg	13	OCT	2020

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
chest pain [Chest pain]
polymorphic rash [Rash]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
(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) 200 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) chronic myeloid leukemia (Chronic myeloid leukaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 19-DEC-2019 / 07-JAN-2020	#1) 20 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	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)
Unknown	Relevant Med History	Tachycardia (Tachycardia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021189020

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
13-DEC-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021189020

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 54-year-old male subject received bosutinib (BOSULIF) at 200 mg daily from 19Dec2019 to 07Jan2020, at 300 mg daily from 08Jan2020 to 18Feb2020, at 400 mg daily from 19Feb2020 to 31Mar2020 and at 500 mg daily from 01Apr2020 and ongoing for chronic myeloid leukaemia. Medical history included chronic myeloid leukemia, exertional tachycardia and post-traumatic left thoracic pain. Concomitant medications were not reported. The patient experienced chest pain on 13Oct2020. The event was assessed medically significant. An electrocardiogram on 14Oct2020 was normal. The patient recovered from the event on 15Oct2020. In Nov2020, the subject complained of pruriginous cutaneous lesions of variable localisation. The event was reported as polymorphic rash, with onset date of 20Nov2020. On 09Dec2020, a skin biopsy was performed and no specific lesions allowing specific diagnosis were found. Skin corticosteroids were prescribed but were slightly effective. The anti-histaminic drugs were ineffective. The patient had not recovered from this event. The events chest pain and polymorphic rash were assessed as non-serious and rated grade 2. The action taken in response to the events for bosutinib was dose not changed.

The investigator considered the event chest pain as neither related to the study drug bosutinib nor to a concomitant medication, and the event polymorphic rash as related to the study drug bosutinib and unrelated to any concomitant medication.

Reporter comment: in the report of 11Jan2021: the patient reports the apparition in Nov2020 of pruritic skin lesions of variable location. A biopsy was performed on 09Dec2020: no specific lesions to suggest a diagnostic. Dermocorticoids were prescribed with low efficacy, antihistamines were not effective. The biopsy did not allow a formal diagnosis. Passage to the emergency room on 14Oct2020 from 7:20 pm to 11:08 pm. Return to home.

Follow-up (13Dec2021): this is a follow-up non-interventional study report (Post Authorization Safety Study) for protocol B1871047. Updated information: event chest pain was assessed as medically significant, bosutinib therapy dates and doses, medical history, reporter's comment. The case has been upgraded to serious.

Case Comment: The reported event chest pain is considered as unrelated to the study drug bosutinib. The patient had a medical history of post-traumatic left thoracic pain. The event polymorphic rash assessed as related to the study drug bosutinib, based on the reasonable temporal association and the known safety profile of bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09-DEC-2020	Biopsy skin	histological lesion not allowing formal diagnosis	
2	14-OCT-2020	Electrocardiogram	normal	

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	08-JAN-2020 / 18-FEB-2020; 1 month 11 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	19-FEB-2020 / 31-MAR-2020; 1 month 13 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	500 mg, daily; Unknown	chronic myeloid leukemia (Chronic myeloid leukaemia)	01-APR-2020 / Ongoing; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Chest pain (Chest pain);

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	FRANCE		PRIVACY		24 Years	Female	58.00 kg	17	DEC	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Fatigue [Fatigue]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL).

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 14-NOV-2018 / 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
MAY-2009 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021192868

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-MAY-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 24-year-old female patient (unknown if pregnant) received bosutinib (BOSUTINIB), since 14Nov2018 (ongoing) at 300 mg 1x/day. The patient's relevant medical history included: "Chronic myeloid leukemia", start date: May2009 (ongoing). The patient's concomitant medications were not reported.
The following information was reported: FATIGUE (non-serious) with onset 17Dec2019, outcome "recovered" (27May2020). The action taken for bosutinib was dosage not changed.

According to the reporter, the event was related to study drug bosutinib but not related to concomitant medication.

Follow-up (10May2022): This is a follow-up report to a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL).
Updated information: Patient's details provided (DOB, height, weight, gender), Medical history (chronic myeloid leukemia), Drug data (start date, dosage and frequency for bosutinib), Action taken (dose not changed) and Causality assessment.

Case Comment: Based on available information, a possible contributory role of the subject drug BOSUTINIB cannot be excluded for the reported event Fatigue.

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	FRANCE		PRIVACY		32 Years	Female	68.00 kg	18	NOV	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Vulvar burning [Genital burning sensation]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL). This is a Non-Interventional Study report with non-serious event 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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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	Relevant Med History	None ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021192909

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-FEB-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 32-year-old female patient received bosutinib at an unknown dose and frequency for an unspecified indication from an unknown date.
Medical history was none.
Concomitant drugs were unspecified.
In consultation report of 23Nov2020 : The subject was briefly hospitalized in emergency on 18Nov2020 for vulvar burning associated to macroscopic lesions. Sample did not reveled herpes, gonocoque or chlamydia infection. Symptoms well improved with Dermoval.
Event was grade 2, non-serious.
Action taken with suspect drug was not reported.
The event was recovered on 23Nov2020.

According to the investigator event was not related to study drug or to concomitant treatments.

Case Comment: Event Vulvar burning is most likely related to an intercurrent or underlying condition and unrelated to suspect drug BOSUTINIB.

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	FRANCE		PRIVACY		75 Years	Male	97.00 kg	07	DEC	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

covid positive [SARS-CoV-2 test positive]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 19-AUG-2020 / 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021196327

24c. DATE RECEIVED BY MANUFACTURER
25-AUG-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male subject was recruited in the above-mentioned study and received bosutinib (BOSULIF), since 19Aug2020 (ongoing) at 300 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported. On 07Dec2020, the patient had COVID-19 test positive rated grade 2. The event was assessed as non-serious. No action was taken with bosutinib in response to the event. The patient had recovered from the event in Dec2020.

The investigator considered the event not related to bosutinib.

No follow-up attempts are needed. No further information expected.

Follow-up(21Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: medical history, start date and dosage for suspect drug bosutinib.

Follow-up attempts are completed. No further information is expected.

Amendment: This follow-up report is being submitted to amend previously reported information: update of the event "covid positive" to "COVID-19 test positive".

Case Comment: In concurrence with the investigator, the reported COVID positive is assessed as unrelated to the study drug, bosutinib. The patient's immunocompromised state and the global pandemic provide an alternative explanation 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	07-DEC-2020	SARS-CoV-2 test Positive	Positive	

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	FRANCE		PRIVACY		75 Years	Male	97.00 kg		AUG	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Diarrhea [Diarrhoea]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 27-FEB-2020 / 18-AUG-2020	#1) 5 months 23 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021196375

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021196375

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), first regimen from 27Feb2020 to 18Aug2020 at 200 mg daily and second regimen since 19Aug2020 (ongoing) at 300 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: DIARRHOEA (non-serious) with onset Aug2020, outcome "recovered" (03Jun2021), described as "Diarrhea". The action taken for bosutinib was dosage not changed.

Clinical course: In the report of 14Dec2020, some diarrhea during treatment with Bosulif 300 mg.

The reporter considered "diarrhea" related to bosutinib.

Follow-up (04Jun2021): New information received from study site includes: Subject's date of birth updated (age remains unchanged), diarrhea resolved on 03Jun2021.

Follow-up (20Apr2022): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information: patient details.
No follow-up attempts are possible. No further information is expected.

Follow-up (21Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information included: medical history, suspect drug data (dosage regimens), clinical course.

Follow-up attempts are completed. No further information is expected.

Case Comment: Assuming the plausible temporal association and considering the known safety profile of bosutinib, the Company cannot completely exclude the possible causality between the reported diarrhea and the administration of the suspect.
The follow up information does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	Unknown	19-AUG-2020 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		70 Years	Female	56.00 kg			2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

CATARACT [Cataract]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 04-SEP-2018 / 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
04-JAN-2011 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021196504

24c. DATE RECEIVED BY MANUFACTURER
27-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 70-year-old female subject started to receive bosutinib (BOSULIF) from 04Sep2018 and ongoing at 200mg daily, for chronic myeloid leukemia. Medical history included chronic myeloid leukemia since 04Jan2011 and ongoing. Concomitant medications, if any, were not reported. On an unknown date in 2019, the subject experienced cataract. The event was rated as grade 2, reported as non-serious. No action was taken in response to this event for bosutinib. On an unknown date in Mar2019, the subject recovered from the event.

The investigator assessed the event cataract as unrelated to bosutinib and unrelated to concomitant medications.

Follow-up (03Dec2021): This is a follow-up non-interventional study report for protocol B1871047. Updated information: medical history added (chronic myeloid leukemia since 04Jan2011 and ongoing).

No follow-up attempt initiated. No further information expected.

Follow-up (27Sep2023): This is a follow-up non-interventional study report for protocol B1871047 received from the clinical team. Updated information: suspect product data (onset date added for bosutinib, ongoing ticked off for bosutinib and dose added).

No follow-up attempts is needed. No further information is expected.

Follow-up (27Sep2023): This is a follow-up non-interventional study report for protocol B1871047 received from the investigator. Updated information: Drug data (bosutinib frequency added).

Case Comment: In concurrence with the investigator, the reported cataract is assessed as unrelated to the study drug, bosutinib. It is most likely an intercurrent condition in this elderly subject.

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	FRANCE		PRIVACY		47 Years	Female	59.50 kg	04	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

COVID infection [COVID-19]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) MAR-2020 / 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021216458

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 2021216458

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 47-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since Mar2020 (ongoing) at 500 mg daily. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
On 04Jan2021, the patient experienced COVID infection, which was considered non-serious, grade 2. No action was taken in response to the event for bosutinib. The outcome of the event was recovered on 12Feb2021.

The investigator considered the event unrelated to the study drug or to concomitant medications.

Follow-up (20Dec2021): This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047 (Study alias BOSEVAL). Updated information: event verbatim term updated to COVID infection, onset date updated to 04Jan2021.

Follow-up (28Jul2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: patient weight and medical history.

Follow-up (28Sep2023): This is a non-interventional follow-up study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information includes: start date and daily dose of BOSULIF and removal of laboratory test: SARS-CoV-2 test.

Case Comment: The reported event of COVID infection is assessed as unrelated to the study drug bosutinib (BOSULIF) or to concomitant medications. The event is possibly favored by the immunosuppressive state associated with the underlying malignancy.

The follow up information 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			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
PRIVACY	FRANCE		PRIVACY		66 Years	Female	Unk	22	AUG	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

asthenia grade 1 [Asthenia]
anxiety grade 1 [Anxiety]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 23-JUL-2019 / 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) PANTOPRAZOLE (PANTOPRAZOLE) ; 08-FEB-2019 / Ongoing
#2) BISOPROLOL (BISOPROLOL) ; Ongoing
#3) EXFORGE (AMLODIPINE BESILATE, VALSARTAN) ; Ongoing
#4) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; 2010 / Ongoing
#5) MEDIATENSYL [URAPIDIL HYDROCHLORIDE] (URAPIDIL HYDRO
#6) PRAVASTATIN (PRAVASTATIN) ; 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	Arterial hypertension (Hypertension)
Unknown	Relevant Med History	Hypercholesterolemia (Hypercholesterolaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021235566

24c. DATE RECEIVED BY MANUFACTURER
22-JUN-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 66-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since 23Jul2019 (ongoing) at 200 mg daily. The patient's relevant medical history included: "Arterial hypertension" (unspecified if ongoing); "Hypercholesterolemia" (unspecified if ongoing); "Hypothyroidism" (unspecified if ongoing); "Fibromyalgia" (unspecified if ongoing). Concomitant medication(s) included: PANTOPRAZOLE oral taken for pain prophylaxis, start date: 08Feb2019 (ongoing); BISOPROLOL oral taken for hypertension (ongoing); EXFORGE oral taken for hypertension (ongoing); LEVOTHYROX oral taken for hypothyroidism, start date: 2010 (ongoing); MEDIATENSYL [URAPIDIL HYDROCHLORIDE]; PRAVASTATIN; VITAMIN B12 [CYANOCOBALAMIN].
The following information was reported: ANXIETY (non-serious) with onset 22Aug2019, outcome "recovered" (Aug2019), described as "anxiety grade 1"; ASTHENIA (non-serious) with onset 16Dec2019, outcome "recovered" (13Dec2021), described as "asthenia grade 1". The action taken for bosutinib was dosage not changed.

The reporter considered "asthenia grade 1" and "anxiety grade 1" not related to bosutinib.

Follow-up (06Dec2022): New information received from investigational site via CRO.
Updated information included: reporter's details, Other Relevant History, Primary Regimen for suspect drug captured (start date, dose, unit, frequency), concomitant medications coded, outcome and stop date for event, causality for asthenia provided.

Follow-up (22Jun2023): New information received from the clinical team.
Updated information: concomitant drug data (updated dose, route, and indication for amlodipine besilate, levothyroxine sodium, and bisoprolol; updated dose, start date, and indication for pantoprazole), company causality confirmed as related for event asthenia.

Follow-up attempts are completed. No further information is expected.

Case Comment: The Company cannot completely exclude the possible causality between the reported asthenia and the administration of bosutinib, based on the reasonable temporal association and the known safety profile of the suspect. Conversely, the reported anxiety is unrelated to bosutinib.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#5) MEDIATENSYL [URAPIDIL HYDROCHLORIDE] (URAPIDIL HYDROCHLORIDE) ; Unknown

#7) VITAMIN B12 [CYANOCOBALAMIN] (CYANOCOBALAMIN) ; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Hypothyroidism (Hypothyroidism);
Unknown	Relevant Med History	Fibromyalgia (Fibromyalgia);

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	FRANCE		PRIVACY		66 Years	Female	Unk			2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

HEMORRHOIDS grade 2 [Haemorrhoids]
Pelvic heaviness grade 1 [Pelvic discomfort]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 23-JUL-2019 / 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) PANTOPRAZOLE (PANTOPRAZOLE) ; Ongoing
#2) BISOPROLOL (BISOPROLOL) ; Ongoing
#3) EXFORGE (AMLODIPINE BESILATE, VALSARTAN) ; Ongoing
#4) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; 2010 / Ongoing
#5) MEDIATENSYL [URAPIDIL HYDROCHLORIDE] (URAPIDIL HYDRO
#6) PRAVASTATIN (PRAVASTATIN) ; 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	Arterial hypertension (Hypertension)
Unknown to Ongoing	Relevant Med History	Hypothyroidism (Hypothyroidism)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021253159

24c. DATE RECEIVED BY MANUFACTURER
06-DEC-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 2021253159

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 66-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since 23Jul2019 (ongoing) at 200 mg daily. Ongoing medical histories included arterial hypertension, hypothyroidism, hypercholesterolemia, and fibromyalgia. Concomitant medications included pantoprazole taken for an unspecified indication from an unspecified start date and ongoing; bisoprolol taken for an unspecified indication from an unspecified start date and ongoing; amlodipine besilate, valsartan (EXFORGE) taken for an unspecified indication from an unspecified start date and ongoing; levothyroxine sodium (LEVOTHYROX) taken for an unspecified indication from 2010 and ongoing; urapidil hydrochloride (MEDIATENSYL) taken for an unspecified indication, start and stop date were not reported; pravastatin taken for an unspecified indication, start and stop date were not reported; and cyanocobalamin (VIT B12) taken for an unspecified indication, start and stop date were not reported. The subject experienced hemorrhoids grade 2 (non-serious) on 2019 with outcome of recovered in 2019 and, pelvic heaviness grade 1 (non-serious) on 2019 with outcome of recovered in 2019. The action taken in response to the events for bosutinib was dose not changed.

The investigator assessed the events hemorrhoids and pelvic heaviness as unrelated to the study drug or concomitant medications.

Follow-up (06Dec2022): This is a non-interventional study follow-up report received from the investigational site via CRO for protocol B1871047.
Updated information: bosutinib therapy details (start date, dose description).

Case Comment: In concurrence with the reporting investigator, the reported events hemorrhoids and pelvic heaviness are considered intercurrent disease, unrelated to the administration of bosutinib. The follow-up information received does not alter the previous company clinical evaluation.

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#5) MEDIATENSYL [URAPIDIL HYDROCHLORIDE] (URAPIDIL HYDROCHLORIDE) ; Unknown

#7) VIT B12 (CYANOCOBALAMIN) ; Unknown

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	Fibromyalgia (Fibromyalgia);

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	FRANCE		PRIVACY		75 Years	Male	97.00 kg	11	MAR	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Water and sodium retention [Fluid retention]
Water and sodium retention [Sodium retention]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 19-AUG-2020 / 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021273229

24c. DATE RECEIVED BY MANUFACTURER
21-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), since 19Aug2020 at 300 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: FLUID RETENTION (non-serious), SODIUM RETENTION (non-serious) all with onset 11Mar2021, outcome "recovered" (Mar2021) and all described as "Water and sodium retention". Relevant laboratory tests and procedures are available in the appropriate section. The event water and sodium retention was considered not serious and rated grade 2. The subject fully recovered from water and sodium retention in Mar2021. The patient had bilateral voluminous oedema of lower limbs, tended, pitting, hepatojugular reflux. In response to water and sodium retention, bosutinib dose was reduced. The patient received furosemide (LASILIX) and had rapid cardiologic consultation for evaluation of left ventricular ejection fraction, repeat electrocardiogram. On 18Mar2021, cardiologist consultation was performed: water retention, iatrogenic / no cardiac cause was reported. The action taken for bosutinib was dosage reduced. Events did not recurred with drug reintroduction. Bosutinib reported as ongoing at the time of the report.

The investigator assessed the event as related to study drug bosutinib and unrelated to concomitant medication.

No follow-up attempt are possible. No further information is expected.

Follow-up (04Jun2021): New information received from investigator via CRO includes: subject's gender, lab data, outcome of the events and investigator comment.

No follow-up attempts are needed. No further information is expected.

Follow-up (20Apr2022): This is a report from a Non-Interventional Study from the investigator site via the CRO.

Updated information includes: action taken of bosutinib updated.

Follow-up (12Jul2023): This is a Non-Interventional Study follow up report from the investigator site via the CRO. Updated information: drug reintroduction details.

Follow-up(21Jul2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: medical history, start date for suspect drug bosutinib.

Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the available information, the company considers that a causal relationship between water and sodium retention and bosutinib cannot be excluded due to plausible temporal association and/or known drug safety profile. 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	18-MAR-2021	Specialist consultation	water retention, iatrogenic / no cardiac cause	

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	FRANCE		PRIVACY		63 Years	Female	111.00 kg		MAR	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

mild sleep apnea syndrome [Sleep apnoea syndrome]
Cervical arthrosis [Spinal osteoarthritis]
Headaches [Headache]
Dry scalp [Dry skin]
Scalp folliculitis [Folliculitis]
Melanonychia of toes [Nail pigmentation]
Urinary infection [Urinary tract infection]
seborrheic keratosis [Seborrhoeic keratosis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF **(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) Bosulif (BOSUTINIB) Film-coated tablet
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 100 mg

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) 12-NOV-2018 / 18-NOV-2018

19. THERAPY DURATION
#1) 7 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021319131

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

A 63-year-old female patient received bosutinib (BOSULIF), first regimen from 12Nov2018 to 18Nov2018 at 100 mg, second regimen from 19Nov2018 to 25Nov2018 at 200 mg, third regimen from 26Nov2018 to 02Dec2018 at 300 mg and fourth regimen since 03Dec2018 (ongoing) at 400 mg. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: NAIL PIGMENTATION (non-serious) with onset Mar2019, outcome "recovering", described as "Melanonychia of toes"; SLEEP APNOEA SYNDROME (non-serious) with onset 21Jun2019, outcome "recovering", described as "mild sleep apnea syndrome"; DRY SKIN (non-serious) with onset Nov2019, outcome "recovered" (2020), described as "Dry scalp"; FOLLICULITIS (non-serious) with onset 26Dec2019, outcome "recovered" (2020), described as "Scalp folliculitis"; SPINAL OSTEOARTHRITIS (non-serious) with onset Apr2020, outcome "recovered" (2020), described as "Cervical arthrosis"; HEADACHE (non-serious) with onset Apr2020, outcome "recovered" (2020), described as "Headaches"; URINARY TRACT INFECTION (non-serious) with onset 26Oct2020, outcome "recovered" (17Nov2020), described as "Urinary infection"; SEBORRHOEIC KERATOSIS (non-serious) with onset 09Dec2021, outcome "recovering", described as "seborrheic keratosis". The action taken for bosutinib was dosage not changed.

The reporter considered "melanonychia of toes" related to bosutinib. The reporter considered "mild sleep apnea syndrome", "cervical arthrosis", "dry scalp", "scalp folliculitis", "urinary infection" and "seborrheic keratosis" not related to bosutinib. The reporter's assessment of the causal relationship of "headaches" with the suspect product(s) bosutinib 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: The event "Melanonychia of toes" and urinary infection were non-serious, grade 2, event mild sleep apnea syndrome was rated grade 1, cervical arthrosis was rated grade 2, dry scalp was rated grade 1, seborrheic keratosis rated grade 2, Scalp folliculitis was rated grade 1.

No follow-up attempts are possible. No further information is expected.

Follow-up (16Dec2021): This is a follow-up non-interventional study report (Post Authorization Safety Study) for protocol B1871047.
Updated information: Patient's gender, date of birth, height and weight added. Event verbatim term "Nail discoloration in the toes" was updated to "Melanonychia of toes", outcome updated to recovering, causality updated to related. New event added: urinary infection.

Follow-up (19Jan2022): This is a follow-up non-interventional study report (Post Authorization Safety Study) for protocol B1871047.
Updated information: patient's date of birth and age, new event "seborrheic keratosis" added, onset date of event mild sleep apnea syndrome and dry scalp, outcome of event mild sleep apnea syndrome updated from not recovered to recovering and of event Scalp folliculitis updated from not recovered to recovered, causality assessment for events mild sleep apnea syndrome, right scaputalgia, cervical arthrosis, dry scalp and scalp folliculitis.

No follow-up attempt initiated. No further information expected.

Follow-up (06Sep2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

Updated information includes: therapy dates and regimens for bosutinib.

Follow-up (06Sep2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: event right scapulalgia was removed.
Follow-up attempts are completed. No further information is expected.

Case Comment: The events mild sleep apnea syndrome, cervical arthrosis, seborrheic keratosis, headaches, dry scalp, scalp folliculitis, and Melanonychia of toes (previously reported as nail discoloration)" more likely represent an intercurrent medical conditions, not related to the suspect product bosutinib. This case will be re-assessed should additional information becomes available.

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) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg; Unknown	Unknown	19-NOV-2018 /

Mfr. Control Number: 2021319131

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
Regimen #2			25-NOV-2018; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg; Unknown	Unknown	26-NOV-2018 / 02-DEC-2018; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg; Unknown	Unknown	03-DEC-2018 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		75 Years	Male	79.00 kg		APR	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

cramps [Muscle spasms]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 06-JUL-2019 / 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		

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021319256

24c. DATE RECEIVED BY MANUFACTURER
28-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 2021319256

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), first regimen since 06Jul2019 at 100 mg daily, second regimen since 16Jul2019 at 200 mg daily, third regimen since 23Jul2019 at 300 mg daily, fourth regimen since 01Aug2019 at 400 mg daily, fifth regimen since 21Aug2019 at 300 mg daily, sixth regimen since 24Apr2020 at 200 mg daily and seventh regimen from 05Nov2020 to 20Oct2022 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: MUSCLE SPASMS (non-serious) with onset Apr2020, outcome "recovered" (Apr2020), described as "cramps". The action taken for bosutinib was dosage reduced.

The causality for event cramps was considered as related to bosutinib by the investigator Causality of hypertension was considered unrelated to bosutinib by the investigator.

Follow-up (02Jun2022): This is a follow-up for a non-Interventional Study source reporting the subject's age and gender, additional event of hypertension, causality assessment between events and study product, and information regarding event outcome.

Follow-up (17Jul2023): This is a follow-up for a non-Interventional Study source from the investigational site via the CRO. Updated information: event hypertension removed.

Follow-up (28Jul2023): This follow-up is received from the clinical team included query response regarding rational of deletion of event hypertension on 11May2021: no aggravated or unbalanced hypertension, confirmed by the investigator. Change of treatment for hypertension following a stock shortage of urapidil (MEDIATENSYL). Dosage regimen of bosutinib updated.

Case Comment: The Company cannot completely exclude the possible causality between the reported cramps and the administration of bosutinib, based on the reasonable temporal association and lacking alternative explanations. This case will be re-assessed should additional information become available.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, daily; Unknown	Unknown	16-JUL-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, daily; Unknown	Unknown	23-JUL-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg, daily; Unknown	Unknown	01-AUG-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #5	300 mg, daily; Unknown	Unknown	21-AUG-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #6	200 mg, daily; Unknown	Unknown	24-APR-2020 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #7	300 mg, daily; Unknown	Unknown	05-NOV-2020 / 20-OCT-2022; 1 year 11 months 16 days

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	FRANCE		PRIVACY		51 Years	Female	98.00 kg		FEB	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

COVID-19 infection [COVID-19]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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	Relevant Med History	none ()
	REFER TO PREVIOUS AEs	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021319277

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 51-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), (ongoing). The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: COVID-19 (non-serious) with onset Feb2020, outcome "recovered" (Mar2020), described as "COVID-19 infection". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.

The reporter considered "covid-19 infection" not related to bosutinib.

Additional information: No concomitant medication was reported. Event COVID-19 infection was rated grade 1 and considered not serious. The investigator assessed this event as unrelated to concomitant drug also.

Investigator's comment: patient was infected by COVID-19 in Feb-Mar2020 with a SARS-Cov-2 serology positive on 25Apr2020 and IgM on 18Jun2020. The patient had not yet did her IgG seroconversion. A PCR test was lately performed in May2020 which was negative.

Follow-up (05Apr2022): This is a follow-up to a non-interventional study for protocol B1871047. Updated information: patient's partial birthdate, gender, height and weight, medical history (no), reaction data (event term, onset date, causality assessment), investigator's comment.

No follow-up attempt initiated. No further information expected.

Follow-up (07Sep2022): This is a non-interventional follow-up study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information included: stop date for Covid-19 (Mar2020).

Follow-up attempts are completed. No further information is expected.

Case Comment: There is not a reasonable possibility to consider the reported COVID-19 infection is related to the administration of the suspect, bosutinib.
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	18-JUN-2020	SARS-CoV-2 antibody test Positive	positive	
2	25-APR-2020	SARS-CoV-2 test Positive	positive	
3	MAY-2020	SARS-CoV-2 test Negative	negative	

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	FRANCE		PRIVACY		75 Years	Female	52.10 kg			2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

anxio depressive syndrome/ Depressive anxiety syndrome was rated grade 1 [Mixed anxiety and depressive disorder]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg/ 200 mg, alternately

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) Unknown / 30-JUN-2022

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	Relevant Med History	none ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021319297

24c. DATE RECEIVED BY MANUFACTURER
30-NOV-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old female patient received bosutinib (BOSULIF), till 30Jun2022 at alternate day (300 mg/ 200 mg, alternately) for chronic myeloid leukaemia. The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: MIXED ANXIETY AND DEPRESSIVE DISORDER (non-serious) with onset 2020, outcome "not recovered", described as "anxio depressive syndrome/ Depressive anxiety syndrome was rated grade 1". The action taken for bosutinib was dosage not changed.
Additional information: There was no mention of progression of the neoplasm.

The reporter considered "anxio depressive syndrome/ depressive anxiety syndrome was rated grade 1" not related to bosutinib.

Follow-up attempts are completed. No further information is expected.

Follow-up (07Sep2023): This is a follow up report combining information from duplicate reports 2021319297 and PV202200059001. The current and all subsequent follow up information will be reported under manufacturer report number 2021319297. The new information reported from a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047 from case PV202200059001 included: new reporter, patient data, suspect product data, Action taken, relationship and clinical information.

Follow-up (24Oct2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: there was no mention of progression of the neoplasm.

Follow-up (14Nov2023): This is a follow-up report from the clinical team Following reconciliation.
Updated information includes: event "lack of efficacy" was removed as no notion of neoplasm progression in the patient's record (site staff replied), event "Cutaneous xerosis" was removed as it was a symptom of scalp itching (refers to AER#2020493488).

Follow-up attempts are completed. No further information is expected.

Follow-up (30Nov2023): This is a follow-up non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information included: event seborrheic keratosis deleted.

Case Comment: Based on available information, the reported anxio depressive syndrome/ Depressive anxiety syndrome is considered unrelated to the study drug, bosutinib.

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	FRANCE		PRIVACY		63 Years	Male	81.00 kg		AUG	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ACHILLES TENDON RUPTURE [Tendon rupture]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047 (Study alias BOSEVAL).

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021325670

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
23-MAR-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 63-years-old male patient received bosutinib (BOSULIF), via an unspecified route of administration from an unspecified date and ongoing, at unspecified dose and frequency for an unspecified indication. The patient's medical history and concomitant medications were not reported. The patient experienced achilles tendon rupture on Aug2019. The event rupture of Achille's heel was reported serious as hospitalization with grade 2. The action taken in response to the event for bosutinib was dose not changed. The outcome of event was recovered on 16Aug2019. According to the investigator, the event was unrelated to bosutinib or to concomitant drugs.

Case Comment: The reported event rupture of Achille's heel was reported serious as hospitalization and is unrelated to the study drug, bosutinib (BOSULIF). This case will be reassessed when further information is provided.

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	FRANCE		PRIVACY		68 Years	Male	103.00 kg	13	SEP	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

EXTRASYSTOLE [Extrasystoles]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.
A 68-year-old male patient received bosutinib (BOSULIF), via an unspecified route of administration from 14Dec2017 to ongoing at 500 mg

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 14-DEC-2017 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021325700

24c. DATE RECEIVED BY MANUFACTURER
16-MAY-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

daily for an unspecified indication. The patient's medical history and concomitant medications were not reported. The patient experienced extrasystole on 13Sep2019. The action taken in response to the event for bosutinib was dose not changed. The outcome of event was not recovered. The reporter considered event extrasystoles was non-serious, grade 1, unrelated to the study drug or concomitant medications.

Follow-up (28Feb2022): This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047.
Updated information included: The event "extrasystoles" was considered as grade 1.

Follow-up (16May2022): new information received from the investigator via the CRO.
Updated information included: suspect product data (dose, frequency, and dates) added

Case Comment: The company concurs with the investigator that the event Extrasystoles was unrelated to bosutinib. Of note, the action taken in response to the event for bosutinib was dose not changed. 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
PRIVACY	FRANCE		PRIVACY		67 Years	Male	86.00 kg			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
Retinal haemorrhage [Retinal haemorrhage]
IRON DEFICIENCY ANEMIA [Iron deficiency anaemia]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP)

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021333797

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-NOV-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

for protocol B1871047.

A 67-year-old male patient received bosutinib (BOSULIF), (ongoing). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: RETINAL HAEMORRHAGE (medically significant) with onset 2019, outcome "recovered" (2020); IRON DEFICIENCY ANAEMIA (non-serious) with onset Oct2019, outcome "recovered" (04Dec2019), described as "IRON DEFICIENCY ANEMIA". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of retinal haemorrhage. The patient experienced retinal haemorrhage on an unspecified date in 2019, rated grade 2, serious (since it required surgery); and iron deficiency anemia in Oct2019, rated grade 3, non-serious. The reporter considered the events were unrelated to the study drug bosutinib. Comment: Hemorrhage operated (no trace of hospitalization).

The reporter considered "retinal haemorrhage" and "iron deficiency anemia" not related to bosutinib.

Follow-up (07Feb2022): This is a follow-up report from a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.
Updated information: outcome of both events was updated and stop date added.

Amendment: This follow-up report is being submitted to amend previous information: gender was updated to male.

Follow-up (14Nov2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from the clinical team in the context of reconciliation for protocol B1871047.
Updated information includes: Seriousness of event retinal haemorrhage was confirmed as serious.

Case Comment: In agreement with the investigator, the reported retinal haemorrhage and iron deficiency anemia are most likely related to intercurrent or underlying conditions and unrelated to suspect drug bosutinib. The action taken of suspect drug was dose not changed and events were resolving.
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
PRIVACY	FRANCE		PRIVACY		58 Years	Male	70.00 kg	06	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Left renal colic [Renal colic]
Left intermittent asymptomatic lithiasis [Lithiasis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 22-JAN-2019 / 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) METFORMIN (METFORMIN) ; Ongoing
#2) VICTOZA (LIRAGLUTIDE) ; 12-APR-2018 / Ongoing
#3) TAHOR (ATORVASTATIN CALCIUM) ; Ongoing
#4) APROVEL (IRBESARTAN) ; 12-APR-2018 / Ongoing
#5) PANTOPRAZOLE (PANTOPRAZOLE) ; 21-JAN-2019 / Ongoing
#6) SMECTA [DIOSMECTITE] (DIOSMECTITE) ; 21-JAN-2019 / 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 currently treated	Diabetes (Diabetes mellitus)
Unknown to Ongoing	Relevant Med History currently treated	Hypercholesterolemia (Hypercholesterolaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021386330

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
20-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 58-year-old male patient received bosutinib (BOSULIF), since 22Jan2019 (ongoing) at 400 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "Diabetes" (ongoing), notes: currently treated; "Hypercholesterolemia" (ongoing), notes: currently treated; "Psoriasis" (ongoing), notes: currently treated; "Neo bladder" (ongoing); "Hypertension arterial" (unspecified if ongoing), notes: currently treated; "Nausea" (ongoing); "Diarrhea" (ongoing), notes: currently treated; "Kidney stones" (ongoing); "Appetite decreased" (unspecified if ongoing). Concomitant medication(s) included: METFORMIN taken for diabetes mellitus (ongoing); VICTOZA taken for diabetes mellitus, start date: 12Apr2018 (ongoing); TAHOR (ongoing); APROVEL taken for hypertension, start date: 12Apr2018 (ongoing); PANTOPRAZOLE taken for gastrooesophageal reflux prophylaxis, start date: 21Jan2019 (ongoing); SMECTA [DIOSMECTITE] taken for prophylaxis against diarrhoea, start date: 21Jan2019 (ongoing); AUGMENTINE [AMOXICILLIN;CLAVULANIC ACID] taken for pneumonia, start date: Feb2019, stop date: 14Feb2019; ROCEPHINE taken for pyrexia, nephritis, start date: Feb2019, stop date: 03Mar2019; ONDANSETRON taken for prophylaxis of nausea and vomiting, start date: 21Feb2019, stop date: 22Feb2019; PARACETAMOL taken for nephritis, start date: 20Feb2019, stop date: 22Feb2019; ACUPAN taken for nephritis, start date: 21Feb2019, stop date: 22Feb2019; CERAT DE GALIEN taken for psoriasis (ongoing).
The following information was reported: RENAL COLIC (hospitalization) with onset 06Jan2021, outcome "recovered" (04Feb2021), described as "Left renal colic"; LITHIASIS (non-serious) with onset 04Feb2021, outcome "recovering", described as "Left intermittent asymptomatic lithiasis". The patient was hospitalized for renal colic (start date: 04Feb2021, discharge date: 15Mar2021, hospitalization duration: 39 day(s)). The patient underwent the following laboratory tests and procedures: examination: (Jan2021) discovery of left intermittent lithiasis; Ureteroscopy: (2021) unknown results. The action taken for bosutinib was dosage not changed..

The reporter considered "left renal colic" and "left intermittent asymptomatic lithiasis" not related to bosutinib.

Additional information: Left renal colic and left intermittent asymptomatic lithiasis were grade 2. The patient was hospitalized from 12Jan2021 to 13Jan2021 for examination and discovery of left intermittent lithiasis and was hospitalized from 04Feb2021 to 15Mar2021 for ureteroscopy.

Follow-up (25Jan2022 and 28Jan2022): This is a follow-up report for a Pfizer sponsored interventional study B1871047. Updated information includes reaction data (onset date of "left renal colic" updated from "08Jan2021" to "06Jan2021", verbatim of "intermittent asymptomatic lithiasis" updated to "right intermittent asymptomatic lithiasis" and outcome updated from "not resolved" to "recovered on 15Mar2021"), medical history and concomitant drugs (previously not reported), seriousness criteria (updated to serious due to hospitalization for event "left renal colic"), and lab data.

Follow-up (22Mar2022). This follow-up is received from the study coordinator. Updated information: verbatim of the event 'right intermittent asymptomatic lithiasis' was updated to 'left intermittent asymptomatic lithiasis'

Follow-up(23Feb2023): New information received from investigational site via CRO included: outcome for 'left intermittent asymptomatic lithiasis' updated to recovering (stop date deleted)

Follow-up (20Jul2023): This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information included: updated start date of Bosulif (from 04Mar2020 to 22Jan2019).

Case Comment: Both reported left renal colic and intermittent asymptomatic lithiasis are deemed intercurrent diseases, unrelated to bosutinib. 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	JAN-2021	Investigation	discovery of left intermittent lithiasis	
2	2021	Ureteroscopy	unknown results	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#7) AUGMENTINE [AMOXICILLIN;CLAVULANIC ACID] (AMOXICILLIN, CLAVULANIC ACID) ; FEB-2019 / 14-FEB-2019

#8) ROCEPHINE (CEFTRIAXONE SODIUM) ; FEB-2019 / 03-MAR-2019

#9) ONDANSETRON (ONDANSETRON) ; 21-FEB-2019 / 22-FEB-2019

#10) PARACETAMOL (PARACETAMOL) ; 20-FEB-2019 / 22-FEB-2019

Mfr. Control Number: 2021386330

ADDITIONAL INFORMATION

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#11) ACUPAN (NEFOPAM HYDROCHLORIDE) ; 21-FEB-2019 / 22-FEB-2019

#12) CERAT DE GALIEN (BEESWAX WHITE, PRUNUS DULCIS OIL) ; Ongoing

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History currently treated	Psoriasis (Psoriasis);
Unknown to Ongoing	Relevant Med History	Bladder repair (Bladder repair);
Unknown	Relevant Med History currently treated	Hypertension arterial (Hypertension);
Unknown to Ongoing	Relevant Med History	Nausea (Nausea);
Unknown to Ongoing	Relevant Med History currently treated	Diarrhea (Diarrhoea);
Unknown to Ongoing	Relevant Med History	Kidney stones (Nephrolithiasis);
Unknown	Relevant Med History	Appetite decreased NOS (Decreased appetite);

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	FRANCE		PRIVACY		73 Years	Male	95.00 kg	07	JUL	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

right popliteal femoral bridge occlusion [Vascular graft occlusion]
increased uric acid [Blood uric acid increased]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 07-JUL-2020 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021446850

24c. DATE RECEIVED BY MANUFACTURER
23-MAY-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

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

A 73-year-old male patient received bosutinib (BOSULIF), since 07Jul2020 (ongoing) at 200 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: BLOOD URIC ACID INCREASED (non-serious) with onset 07Jul2020, outcome 'recovered' (21Sep2021), described as 'increased uric acid'; VASCULAR GRAFT OCCLUSION (hospitalization) with onset 06Apr2021, outcome 'not recovered', described as 'right popliteal femoral bridge occlusion'. The patient underwent the following laboratory tests and procedures: Echocardiogram: aggravation of the arteriopathy of the lower limbs, notes: Accentuation of walking disorder, echo-doppler showing an aggravation of the arteriopathy of the lower limbs with stage ii arteriopathy for a walking distance LT 100 m, the right femoro-popliteal bypass is unfortunately occluded. Scheduled surgical appointment. Limited internal carotid stenosis. The action taken for bosutinib was dosage not changed.

The reporter considered 'right popliteal femoral bridge occlusion' and 'increased uric acid' not related to bosutinib or to any concomitant drug.

Additional information: The event Vascular graft occlusion was rated grade 3. Event reported as serious.. The started date of bosutinib also reported on 08Jul2020.

Follow-up (01Mar2023): This is a follow-up report from a Non-Interventional Study source for Protocol ID: B1871047. Updated information includes: Bosulif start date updated from 04Apr2018 to 07Jul2020.

Follow-up (06Mar2023): This is a follow up non-interventional study report received from investigational site via CRO.
Updated information included: new event 'increased uric acid' added, onset date of lower limb arteriopathy, outcome of event lower limb arteriopathy updated from not recovered to unknown, causality for event lower limb arteriopathy updated as related to bosutinib (previously unrelated), lab data.

Follow-up (23Mar2023): new information received from investigational site.
Updated information: outcome of Arteriopathy updated.

Follow-up (24Mar2023): This is a follow up non-interventional study report received from investigational site.
Updated information included: Event description changed from 'lower limb arteriopathy' to 'right popliteal femoral bypass occlusion', additional reporter added.

Follow-up (23May2023): This is a follow up non-interventional study report received from investigational site via CRO.
Updated information included: for the event Vascular graft occlusion seriousness criteria of hospitalization added, causality updated from related to unrelated.

Case Comment: Based on the available information, the Company considers the reported events 'right popliteal femoral bypass occlusion', increased uric acid, are unrelated to suspect drug bosutinib and more likely due to underlying or inter-current medical condition.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Echocardiogram	aggravation of the arteriopathy of the lower limbs	
		Accentuation of walking disorder, echo-doppler showing an aggravation of the arteriopathy of the lower limbs with stage ii arteriopathy for a walking distance < 100 m, the right femoro-popliteal bypass is unfortunately occluded. Scheduled surgical appointment. Limited internal carotid stenosis.		

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	FRANCE		PRIVACY		56 Years	Male	73.00 kg	08	APR	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

pleural effusion [Pleural effusion]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047, Study alias BOSEVAL.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, 1x/day	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 14-MAY-2018 / 13-JUN-2018	#1) 1 month

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ALLOPURINOL (ALLOPURINOL) ; Ongoing
#2) TAHOR (ATORVASTATIN CALCIUM) ; Ongoing
#3) HYDROCORTISONE (HYDROCORTISONE) ; Ongoing
#4) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; Ongoing
#5) TESTOSTERONE HEPTANOATE (TESTOSTERONE HEPTANOATE) Injection ; 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	Panhypopituitarism (Hypopituitarism)
Unknown to Ongoing	Relevant Med History	Hypercholesterolemia (Hypercholesterolaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021490742

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-APR-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021490742

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a Non-Interventional Study report with non-serious event only.
A 56-years-old male subject received bosutinib (BOSULIF), via an unspecified route of administration from 14May2018 to 13Jun2018, at 200 mg, once daily, via an unspecified route of administration from 14Jun2018 to 20Apr2021 at 300 mg, once daily for an unspecified indication. Medical history included ongoing panhypopituitarism and ongoing hypercholesterolemia. Concomitant medications included allopurinol taken for panhypopituitarism from an unspecified start date and ongoing; atorvastatin calcium (TAHOR) taken for hypercholesterolemia from an unspecified start date and ongoing; hydrocortisone taken for panhypopituitarism from an unspecified start date and ongoing; levothyroxine sodium (LEVOTHYROX) taken for panhypopituitarism from an unspecified start date and ongoing; testosterone heptanoate taken for an unspecified indication from an unspecified start date and ongoing. The subject experienced pleural effusion on 08Apr2021. Event pleural effusion was reported as non serious, grade 1. Before a gradual dyspnoea appearance in 15 days, chest x-ray requested by the doctor. Chest x-ray of 08Apr2021: bilateral pleural outflow but predominant on the right. Set up treatment with furosemide 40 mg/day from 08Apr2021 to 15Apr2021. Chest x-ray check on 19Apr2021: left basal pleural effusion disappearance and very clear regression right pleural effusion (filling of the bottom of costo-diaphragmatic bag g). Hematology consultation on 20Apr2021: discreet decrease in vesicular murmure right base, decision to stop of treatment with bosulif because criteria for test stopping and recurrent pleural effusion, no therapeutic relay. In response to the event BOSULIF was withdrawn. The outcome of the event was recovering.

The investigator considered that the event was related to Bosulif and unrelated to concomitant medications.

Case Comment: Based on the known drug safety profile and temporal relationship, a causal association between bosutinib and the reported pleural effusion cannot be excluded.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-APR-2021	Chest X-ray bilateral pleural outflow but predominant on the right	bilateral pleural outflow but predominant on the r	
2	19-APR-2021	Chest X-ray left basal pleural effusion disappearance and very clear regression right pleural effusion (filling of the bottom of costo-diaphragmatic bag g).	left basal pleural effusion disappearance and very	

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, 1x/day; Unknown	Unknown	14-JUN-2018 / 20-APR-2021; 2 years 10 months 7 days

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	FRANCE		PRIVACY		77 Years	Female	Unk	02	FEB	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Knee pain [Arthralgia]
Sleep apnea [Sleep apnoea syndrome]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 23-OCT-2020 / 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	Relevant Med History	None ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021523772

24c. DATE RECEIVED BY MANUFACTURER
24-JAN-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 77-year-old female subject received bosutinib (BOSULIF), since 23Oct2020 (ongoing) at 200 mg 1x/day. Subject did not have any medical history. The patient's concomitant medications were not reported. The patient experienced sleep apnea grade 1 on 02Feb2021. On 02Feb2022, Total left knee prosthesis on 02Nov2021 was reported, rated as grade 3 and which required hospitalization. On 03Feb2022, event "Total left knee prosthesis" was updated to "Knee pain" with onset date in 2021. The action taken in response to the event for bosutinib was dose not changed. The outcome of the event sleep apnea grade was not resolved. Knee pain resolved on 15Dec2021.

The investigator considered there was not a reasonable possibility that the events "sleep apnea" and "knee pain" were related to bosutinib.

Follow-up (02Feb2022 and 03Feb2022): This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047. Updated information: Action taken updated to "Dose not changed". New event "Knee pain" added. Case upgraded to serious in this follow-up.

No follow-up attempts are possible. No further information is expected.

Follow-up (24Jan2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information included: start date and dosage for study drug bosutinib.

No follow-up attempts are possible. No further information is expected.

Case Comment: In concurrence with the reporting investigator, the Company deems the reported events knee pain and sleep apnea grade 1 unrelated to the suspect, bosutinib, administration.

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	FRANCE		PRIVACY		67 Years	Male	63.00 kg	06	MAR	2021

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
Myalgia [Myalgia]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for Protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 100 to 500 mg, 1x/day

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) 08-AUG-2019 / 19-AUG-2020

19. THERAPY DURATION
#1) 1 year 12 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) CORTANCYL (PREDNISONE) ; 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	Pseudopolyarthritis (Polymyalgia rheumatica)
21-JUL-2017 to Unknown	Relevant Med History	Chronic myelogenous leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021527532

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
22-APR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021527532

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old male subject received bosutinib (BOSULIF), via an unspecified route of administration from 08Aug2019 to 19Aug2020, at 100 to 500 mg, once daily, via an unspecified route of administration from 20Aug2020 and ongoing, at 500 mg, once daily for an unspecified indication. Medical history included pseudopolyarthritis, chronic myelogenous leukemia from 21Jul2017. Concomitant medication included prednisone (CORTANCYL) taken for pseudopolyarthritis from an unspecified start date and ongoing. The subject experienced myalgia on 06Mar2021 06:30. On 06Mar2021, 06:30 AM, the subject had left leg intense pain with functional impotence. He was taken to the emergencies by her wife, he arrived at 10:45 AM and he left at 04:15 PM. The subject underwent lab tests and procedures which included arterio-venous doppler on 06Mar2021 which was normal and no venous thrombosis was reported. Therapeutic measures were taken as a result of myalgia which included: oxycodone hydrochloride (OXYNORMORO), 5 mg oral, once per day and paracetamol (manufacturer unknown), 1 g, once per day. The subject returned home with a final diagnosis of myalgia which was rated grade 3. Treatment when the subject was discharged, was diazepam (VALIUM), 2 mg if pain. The subject had recovered from the event on 07May2021. The action taken in response to the event for bosutinib was dose not changed.

The event myalgia was confirmed as medically significant as the subject went to the emergency.
According to the investigator, the event was unrelated to study drug bosutinib and to concomitant drug.

Follow-up (15Dec2021): New information received from a contactable investigator from the Non-Interventional Study source for Protocol B1871047.
Updated information: Event myalgia was updated from nonserious to serious (medically significant).

Follow-up (22Apr2022): This is a non-interventional study follow-up report received from the investigational site for protocol B1871047. Updated information confirmation of seriousness.

Case Comment: In concurrence with the investigator, the reported myalgia is unrelated to the study drug, bosutinib. It is mostly likely an intercurrent condition. Of note, the event occurred more than 18 months after start of treatment and resolved without any modification in the administration of bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	06-MAR-2021	Ultrasound Doppler	Normal, No venous 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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	500 mg, 1x/day; Unknown	Unknown	20-AUG-2020 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		78 Years	Male	83.00 kg	03	JUL	2020

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
Prostatic adenocarcinoma, hormone sensible, with bone metastases [Second primary malignancy]
Prostatic adenocarcinoma, hormone sensible, with bone metastases [Prostate cancer metastatic]
Micturition burning [Dysuria]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosulif (BOSUTINIB) Film-coated tablet
(Continued on Additional Information Page)

15. DAILY DOSE(S)
#1) 100 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 01-APR-2019 / 14-APR-2019

19. THERAPY DURATION
#1) 14 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	Prostate adenoma (Prostatic adenoma)
17-JUL-2020 to 11-AUG-2020	Relevant Med History	Urinary retention (Urinary retention)
	suspicion of cancer, required persistent catheterization	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021664469

24c. DATE RECEIVED BY MANUFACTURER
29-JUN-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

A 78-year-old male subject received bosutinib (BOSULIF), from 01Apr2019 to 14Apr2019, at 100 mg, once daily; from 15Apr2019 to 02Jul2019, at 200 mg, once daily; from 03Jul2019 to 07Mar2021, at 300 mg, once daily; and from 08Mar2021 and ongoing at 200 mg, once daily, all via an unspecified route of administration for an unspecified indication. Medical history included ongoing benign hypertrophy of prostate and acute urinary retention from 17Jul2020 to 11Aug2020 with a suspicion of cancer and required persistent catheterization. The subject's concomitant medications were not reported. The subject experienced prostatic adenocarcinoma, hormone sensible, with bone metastases on 03Sep2020. The subject experienced Micturition burning on 03Jul2020. The subject underwent lab tests and procedures which included prostate biopsy on 03Sep2020 which showed prostatic adenocarcinoma hormone sensible, with bone metastases from the beginning; bone scintigraphy on 19Nov2020 which showed condensation and intense hyperfixation of the upper part of the right iliac wing, of the right iliac wing opposite the sacroiliac and of the right crowned aileron in favor of secondary locations; Eastern Cooperative Oncology Group performance status: 0 on an unknown date; histology on 03Sep2020 which showed prostatic adenocarcinoma GLEASON 7 (4 + 3) (90% grade 4) ISUP 3 on 20% of the shavings; Pelvic magnetic resonance imaging on 18Aug2020 which showed PIRADS 5 lesion on the right, 23mm long axis, in contact with the urethra with capsular bulging without sign crossing. Some external iliac nodes without pathological lymphadenopathy; Prostatic specific antigen (PSA) on 25Jul2020: 5.7 ng/ml and 3.16 ng/ml on 10Nov2020, weight: 81 kg on an unknown date on examination. The action taken in response to the event for bosutinib was dose not changed. Therapeutic measures were taken as a result of prostatic adenocarcinoma, hormone sensible, with bone metastases. The outcome of the events Prostatic adenocarcinoma, hormone sensible, with bone metastases was not recovered. The outcome of Micturition burning was resolved on Jul2020.

The investigator considered the event Prostatic adenocarcinoma, hormone sensible, with bone metastases as non-serious (grade 3) and there was not a reasonable possibility that the event was related to the study medication bosutinib or to concomitant treatments. The investigator considered the event Micturition burning as non-serious (grade 1) and there was not a reasonable possibility that the event was related to the study medication bosutinib or to concomitant treatments.

Follow-up (14Dec2021 and 15Dec2021): This is a Non-Interventional Study follow-up report from the clinical team.
Updated information: new event (Micturition burning).

Follow-up (29Jun2023): This is a Non-Interventional Study follow-up report from investigational site via CRO. Updated information includes: Medical history acute urinary retention start date updated to 17Jul2020.

Case Comment: In concurrence with the investigator, the reported "prostatic adenocarcinoma, hormone sensible, with bone metastases", as a second primary malignancy, is deemed unrelated to the study drug, bosutinib. Micturition burning considered symptom of Prostate cancer metastatic, unrelated to bosutinib, as well.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	03-SEP-2020	Biopsy	prostatic adenocarcinoma	
		prostatic adenocarcinoma hormone sensible, with bone metastases from the beginning.		
2	19-NOV-2020	Bone scan	condensation and intense hyperfixation	
		condensation and intense hyperfixation of the upper part of the right iliac wing, of the right iliac wing opposite the sacroiliac and of the right crowned aileron in favor of secondary locations		
3		Eastern Cooperative Oncology Group performance status	0	
4	03-SEP-2020	Histology	prostatic adenocarcinoma GLEASON 7 (4 + 3)	
		prostatic adenocarcinoma GLEASON 7 (4 + 3) (90% grade 4) ISUP 3 on 20% of the shavings		
5	18-AUG-2020	Magnetic resonance imaging pelvic	PIRADS 5 lesion on the right, 23mm long axis	

Mfr. Control Number: 2021664469

ADDITIONAL INFORMATION

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		PIRADS 5 lesion on the right, 23mm long axis, in contact with the urethra with capsular bulging without sign crossing. Some external iliac nodes without pathological lymphadenopathy		
6	25-JUL-2020	Prostatic specific antigen	5.7 ng/ml	
7	10-NOV-2020	Prostatic specific antigen	3.16 ng/ml	
8		Weight	81 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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, 1x/day; Unknown	Unknown	15-APR-2019 / 02-JUL-2019; 2 months 18 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, 1x/day; Unknown	Unknown	03-JUL-2019 / 07-MAR-2021; 1 year 8 months 5 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	200 mg, 1x/day; Unknown	Unknown	08-MAR-2021 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		47 Years	Female	59.50 kg		JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Vocal cords nodule [Vocal cord thickening]
blocked ear sensation [Ear discomfort]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) MAR-2020 / 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021675275

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 47-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since Mar2020 (ongoing) at 500 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: VOCAL CORD THICKENING (hospitalization) with onset Jun2020, outcome "recovered" (26Aug2021), described as "Vocal cords nodule"; EAR DISCOMFORT (non-serious) with onset Feb2021, outcome "recovered" (18Oct2021), described as "blocked ear sensation". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of vocal cord thickening.
Additional information: The dysphonia was rated grade 2 and blocked ear sensation was rated grade 1.
The site stated: in the report of 07Jun2021 dysphonia was noted (polyps of the vocal cords with a surgery to be planned), and sensation of blocked ears. In the report of 22Feb2021, dysphonia was noted since 7-8 months (ENT assessment was reassuring). Patient had surgery of vocal cords nodule on 26Aug2021.

The reporter considered "vocal cords nodule" and "blocked ear sensation" not related to bosutinib.

Follow-up (25Oct2021 and 07Jan2022): This is a follow-up for a report from a Non-Interventional Study source for Protocol B1871047.
Information updated: onset date, outcome and stop date of dysphonia; treatment for dysphonia.

Follow-up (30May2023): This is a follow-up for a report from a Non-Interventional Study received from investigational site via CRO.
Updated information: event onset date and stop date updated.

Follow-up (28Jul2023): This is a follow-up report from the investigator via CRO.
Updated information included: medical history (chronic myeloid leukemia).

Follow-up (28Sep2023): new information received from Clinical team.
Updated information included: Query response (confirmed: it was reported dysphonia is a symptom of the vocal cords nodule. Vocal cords nodule has been recorded as the main event. As a surgery occurred on 26Aug2021 to remove the nodule, the AE has been turned into a Serious Adverse Event with Hospitalization as the seriousness criteria.

Follow-up (28Sep2023): This is a follow-up report from the investigator via CRO. Updated information included: bosutinib details.

Case Comment: The reported events, Vocal cord thickening and blocked ear sensation are deemed intercurrent diseases, unrelated to the study drug, bosutinib. 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
PRIVACY	FRANCE		PRIVACY		61 Years	Male	Unk	06	MAY	2021

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
pericardial effusion [Pericardial effusion]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a report from a Non-Interventional Study source for protocol B1871047, study alias BOSEVAL.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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)
#1) ENTECAVIR (ENTECAVIR) ; Ongoing

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
01-JUN-2000 to Ongoing	Relevant Med History	Renal failure (Renal failure)
01-JAN-2005 to Ongoing	Relevant Med History	Hepatitis B (Hepatitis B)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021759182

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-NOV-2021

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 2021759182

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 61-year-old male subject started to receive bosutinib (BOSULIF, tablet) on an unspecified date, dose, frequency and route of administration for an unspecified indication. Relevant medical history included ongoing mild renal failure since 01Jun2000 and ongoing old hepatitis B since 01Jan2005. Concomitant medications included ongoing entecavir for hepatitis B. On 06May2021, the subject experienced pericardial effusion. The event was rated grade 2 and assessed as medically significant. Ultrasound on 06May2021 found pericardial effusion. Outcome of the event was recovered on an unspecified date in May2021. No action was taken for bosutinib in response to the event.

According to the reporter, the event was related to bosutinib and unrelated to concomitant drug.

Follow-up (25Oct2021): New information reported includes an update about relevant medical history and causality assessment for concomitant medication.

Follow-up (05Nov2021): New information received from the investigational site via CRO includes: Event onset date was updated to 06May2021 (previously 14Jun2021), outcome was updated to recovered (previously recovering).

Case Comment: Based on the known drug safety profile, a contributory role of bosutinib to the reported pericardial effusion cannot be excluded. 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-MAY-2021	Ultrasound scan	pericardial effusion	

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	FRANCE		PRIVACY		59 Years	Female	118.00 kg		DEC	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

abdominal pain [Abdominal pain]
Diarrhea [Diarrhoea]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, 1x/day	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 25-SEP-2018 / 07-DEC-2020	#1) 2 years 2 months 13 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021769940

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old female patient received bosutinib (BOSULIF), first regimen from 25Sep2018 to 07Dec2020 at 200 mg 1x/day and second regimen since 08Dec2020 at 300 mg 1x/day. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: DIARRHOEA (non-serious) with onset Dec2020, outcome "recovered" (12Oct2021), described as "Diarrhea"; ABDOMINAL PAIN (non-serious) with onset Dec2020, outcome "recovered" (12Oct2021). The action taken for bosutinib was dosage reduced.

The reporter considered "abdominal pain" and "diarrhea" related to bosutinib.

Additional information: The events diarrhea and abdominal pain were reported as non-serious with grade 2. As of 03Dec2021, medical report included failure of increase of bosutinib 300 mg with diarrhea, abdominal pain and soft abdomen from 12Oct2021. In response to the event, bosulif was reduced to 200 mg daily on 31Mar2021.

According to the investigator, both events were related to study drug bosutinib and unrelated to concomitant drugs.

Follow-up (03Dec2021): New information received from the investigator via the CRO included reaction data (outcome of events diarrhea and abdominal pain updated to recovered on 12Oct2021) and additional information.

No follow-up attempt initiated. no further information expected.

Follow-up (12Jul2023): New information received from the investigator via the CRO included: new reporter (slide #2), Dechallenge and Rechallenge Results for suspect drug.

Follow-up (24Jul2023): This is a follow up non-interventional study report received from the CRO.
Updated information included: last name of second reporter.

Follow-up (28Jul2023): This is a follow up non-interventional study report received from the CRO.
Updated information included: None was removed from patient's medical history.

Follow-up (27Sep2023): This is a non-interventional study follow-up for protocol B9991045 received from the investigator site via the CRO. Updated information: medical history (ongoing chronic myeloid leukemia) and dosage regimen of bosutinib.

Follow-up (05Oct2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: clinical course details.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the reasonable temporal association and considering the known safety profile of bosutinib, the Company cannot completely exclude the possible causality between the reported diarrhea and abdominal pain and the administration of the suspect.
The follow-up information received does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, 1x/day; Unknown	Unknown	08-DEC-2020 / Unknown; 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
PRIVACY	FRANCE		PRIVACY		72 Years	Female	56.00 kg	21	JUN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Epigastralgia [Abdominal pain upper]
Diarrhea 1x/day [Diarrhoea]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) FLUVASTATINE [FLUVASTATIN] (FLUVASTATINE [FLUVASTATIN]) **(Continued on Additional Information Page)**

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 200 mg, daily	#1) Unknown
#2) UNK	#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 04-SEP-2018 / 04-FEB-2020	#1) 1 year 5 months 1 day
#2) Ongoing	#2) 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	Relevant Med History	None ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021773818

24c. DATE RECEIVED BY MANUFACTURER
27-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 72-year-old female patient received bosutinib (BOSULIF), first regimen from 04Sep2018 to 04Feb2020 at 200 mg daily, second regimen from 05Feb2020 to 07Mar2021 at 300 mg daily and third regimen since 08Mar2021 (ongoing) at 400 mg daily; fluvastatine [fluvastatin] (FLUVASTATINE [FLUVASTATIN]), (ongoing) (Batch/Lot number: unknown). The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: DIARRHOEA (non-serious) with onset 21Jun2021, outcome "recovering", described as "Diarrhea 1x/day"; ABDOMINAL PAIN UPPER (non-serious) with onset 21Jun2021, outcome "recovered" (14Oct2021), described as "Epigastralgia". The action taken for bosutinib was dosage reduced; for fluvastatine [fluvastatin] was dosage not changed.
Additional information: The patient experienced epigastralgia on 21Jun2021 which resolved on 14Oct2021, diarrhea 1x/day on 21Jun2021. The events epigastralgia rated with grade 2 and diarrhea rated with grade 1 were reported as non serious. Since the last consultation, liquid stools once a day. Epigastralgia just after the intake of drugs bosutinib and fluvastatin. The event diarrhea was resolved on 20Mar2023. No action was taken with fluvastatin in response to epigastralgia while bosutinib dose was reduced in response to epigastralgia. No action taken with bosuitnib in response to diarrhea. Event did not reappeared with reintroduction of medication. Bosutinib reported as ongoing at the time of the report.

According to the reporter, epigastralgia was related to study drug bosutinib and related to co-suspect medication fluvastatine while diarrhea was related to bosutinib but not related to fluvastatine.

Follow-up (19May2023): This is a non-interventional study follow-up report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information included: The patient had no medical history. Bosutinib was taken at 200 mg until 04Feb2020 then at 300 mg. Epigastralgia resolved on 14Oct2021. No action was taken with fluvastatin in response to epigastralgia while bosutinib dose was increased.

Follow-up (23May2023): This is a non-interventional study follow-up report received from CRO for protocol B1871047.
Updated information included: updated outcome for diarrhea and recovery date, updated action taken with bosutinib.

Follow-up (12Jul2023): This is a non-interventional study follow up report from same contactable other HCP. Updated information: bosutinib reintroduction details.

Follow-up (27Jul2023): This is a non-interventional study follow-up report received from CRO for protocol B1871047.
Updated information included: Investigator Initial Aware Date, suspect drug Bosulif details (ongoing selected), event Diarrhoea details (stop date, outcome).

Follow-up attempts are completed. No further information is expected.

Case Comment: Due to a reasonable drug-event temporal association and the known drug safety profile, the company deems there is a reasonable possibility that epigastralgia and diarrhea are related to the suspect drug bosutinib. The follow-up information received does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	Unknown	05-FEB-2020 / 07-MAR-2021; 1 year 1 month 3 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg, daily; Unknown	Unknown	08-MAR-2021 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		32 Years	Female	68.00 kg	03	JUN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Unplanned pregnancy [Maternal exposure during pregnancy]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

A 32-year-old female subject (pregnant) received bosutinib (BOSULIF)

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) chronic myeloid leukaemia (Chronic myeloid leukaemia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 19-NOV-2019 / 25-DEC-2019	#1) 1 month 7 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) OPTIMIZETTE (DESOGESTREL) ; Unknown

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
24-MAY-2021		Date of LMP for pregnancy
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)
26-SEP-2017 to Unknown	Relevant Med History	Immune thrombocytopenia (Immune thrombocytopenia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
2021857275

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-FEB-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(Batch/Lot number was not reported), via an unspecified route of administration, from 19Nov2019 to 25Dec2019 at 200 mg daily, from 26Dec2019 to 30Dec2019 at 300 mg daily, from 31Dec2019 to 17Dec2020 at 200 mg daily, and from 18Dec2020 to 23Jun2021 at 300 mg daily (taken intermittently since May2021 - 12 tablets of 100 mg between 01Jun and 23Jun2021), for chronic myeloid leukaemia. Medical history included chronic myeloid leukaemia from an unknown date and ongoing, corticosensitive immunological thrombopenia from 26Sep2017 to an unknown date. The subject had had 2 pregnancies without complication, one abortion on 26Jul2017, one healthy child born on 13Sep2019, with vaginal delivery /Child APGAR 10. Concomitant medication(s) included desogestrel (OPTIMIZETTE) taken for contraception, start and stop date were not reported. The subject experienced unplanned pregnancy on 03Jun2021. The event unplanned pregnancy was rated grade 3. It was "accidental" pregnancy under optimizette, oral contraception. The estimation conception date was May2021 and date of last menstrual period was 24May2021. The patient is expected to deliver one baby on 28Feb2022. Pregnancy was declared following human chorionic gonadotropin (HCG) and ultrasound results. HCG was 2001.0 IU/L on 24Jun2021, commented as pregnancy 4 to 5 weeks. Ultrasound scan on 29Jun2021 revealed monoembryonic pregnancy, 5 weeks of amenorrhea. The subject did not smoke, drink alcohol, use illicit drugs during this pregnancy. The subject stopped bosutinib definitely when she made beta HCG on 24Jun2021. But bosutinib was taken intermittently since May2021 - 12 tablets of 100 mg between 01Jun and 23Jun2021. The subject was seen the hematologist on 01Jul2021, bosutinib was withdrawn on prescription. The action taken in response to the event for bosutinib was permanently withdrawn. The outcome of the unplanned pregnancy was resolved on 22Feb2022.

Reporter's comment: "delivery on 22Feb2022".

The investigator assessed the event as not related to bosutinib.

Follow-ups (29Oct2021): This is a non-interventional study report for protocol B1871047. Updated information includes: event onset date, and bosutinib stop information.

Follow-up (13Jul2022): This is a non-interventional study follow-up report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: the outcome of the event and reporter's comment.

Follow-up (10Feb2023): This is a non-interventional study follow up report for protocol B1871047.
Updated information includes: update start date of bosutinib (19Nov2019) and event unplanned pregnancy (03Jun2021).

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	24-JUN-2021	Human chorionic gonadotropin Pregnancy 4 to 5 weeks	2001.0 IU/l	
2	29-JUN-2021	Ultrasound scan Gestational age 5 weeks of amenorrhea	Monoembryonic pregnancy	

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	chronic myeloid leukaemia (Chronic myeloid leukaemia)	26-DEC-2019 / 30-DEC-2019; 5 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	chronic myeloid leukaemia (Chronic myeloid leukaemia)	31-DEC-2019 / 17-DEC-2020; 11 months 17 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	300 mg, daily (taken intermittently since May2021 - 12 tablets of	chronic myeloid leukaemia (Chronic myeloid leukaemia)	18-DEC-2020 / 23-JUN-2021; 6 months 6 days

Mfr. Control Number: 2021857275

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
	100 mg between 01Jun and 23Jun2021); Unknown		

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Pregnancy (Pregnancy); 1 Abortion on 26Jul2017, 1 healthy child born on 13Sep2019, with vaginal delivery /Child APGAR 10

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	FRANCE		PRIVACY		33 Years	Male	115.00 kg	01	APR	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Benign vertigo [Vertigo]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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
12-OCT-2018 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200012620

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
27-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 33-year-old male patient received bosutinib (BOSULIF), (ongoing) at 500 mg 1x/day. The patient's relevant medical history included: "Chronic myeloid leukemia", start date: 12Oct2018 (ongoing). The patient's concomitant medications were not reported. The following information was reported: VERTIGO (non-serious) with onset 01Apr2021, outcome "recovered" (08Apr2021), described as "Benign vertigo". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of vertigo.

The reporter considered "benign vertigo" not related to bosutinib.

Additional information: The event benign dizziness was reported as non-serious with grade 2. Benign paroxystic dizziness a few days, recovered with an unspecified drug and swing test (rehabilitation of the internal ear).

Follow-up (27Oct2023): This follow-up report is being submitted to amend previously transmitted information following reconciliation between safety and clinical databases: Event term coding was updated: Benign vertigo (previously coded as Benign dizziness).

Case Comment: Based on the information provided, upon FU, the event vertigo is assessed as unrelated to bosutinib. No action was taken for bosutinib 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	FRANCE		PRIVACY		73 Years	Male	96.00 kg		DEC	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

anemia [Anaemia]
STOMACH ACHES [Abdominal pain upper]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) INEXIUM [ESOMEPRAZOLE MAGNESIUM] (ESOMEPRAZOLE MAGNESIUM)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Unknown
#2) UNK	#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown	#1) Unknown
#2) Unknown	#2) 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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200082520

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old male patient received bosutinib (BOSULIF); esomeprazole magnesium (INEXIUM [ESOMEPRAZOLE MAGNESIUM]), (Batch/Lot number: unknown). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ABDOMINAL PAIN UPPER (non-serious) with onset Dec2019, outcome "recovered" (24Feb2020), described as "STOMACH ACHES"; ANAEMIA (non-serious) with onset 23Jan2020, outcome "recovering", described as "anemia". The action taken for bosutinib was dosage reduced; for esomeprazole magnesium was dosage not changed.

The reporter considered "anemia" and "stomach aches" related to bosutinib.

Additional information: The anemia resulted in headaches and fatigue. Anemia was rated grade 2. In response to anemia, bosutinib dose was reduced and no action taken for concomitnat drug INEXIUM. Anemia was related to bosutinib and to concomitant drug INEXIUM. Stomach aches as rated grade 2, related to bosutinib and unrelated to any concomitant drug. No action was taken for bosutinib in response to stomach aches.

No follow-up attempts are needed. No further information is expected.

Case Comment: A causal association between administration of bosutinib and the onset of "anemia" and "stomach aches" cannot be excluded, considering the temporal association and the known adverse event profile of the suspect product.

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	FRANCE		PRIVACY		74 Years	Male	96.00 kg	28	SEP	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

tremor of extremities [Tremor]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report received from a contactable reporter(s) (Physician) for protocol B1871047.

A 74-year-old male patient received bosutinib (BOSULIF).

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200082549

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200082549

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: TREMOR (non-serious) with onset 28Sep2021, outcome "recovered" (03Nov2021), described as "tremor of extremities". The action taken for bosutinib was dosage not changed.
The reporter considered "tremor of extremities" not related to bosutinib.
Additional information: the event was reported as non-serious and rated grade 1.

No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the information currently provided, the company deemed that there is not a reasonable possibility that the event tremor of extremities was related to Pfizer study drug BOSUTINIB.

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	FRANCE		PRIVACY		74 Years	Male	96.00 kg		APR	2021

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
Thoracic pain [Chest pain]
Cardiac insufficiency [Cardiac failure]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200083080

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200083080

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

B1871047.

A 74-year-old male patient received bosutinib (BOSULIF). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: CHEST PAIN (medically significant) with onset Apr2021, outcome "recovered" (01Jun2021), described as "Thoracic pain"; CARDIAC FAILURE (non-serious) with onset Jun2021, outcome "not recovered", described as "Cardiac insufficiency". The patient underwent the following laboratory tests and procedures: Angiocardiogram: (17May2021) stenosis of interior intraventricular artery 2=40%, notes: and right coronary 50%. The action taken for bosutinib was dosage not changed.

Additional information: thoracic pain (effort angor): exploration coronarography on 07May2021: stenosis of Anterior intraventricular artery 2=40% and right coronary 50%. Multifactor cardiac insufficiency (ischemic and hypertension) leading to edema, hypertension arterial, fatigue and renal insufficiency. Thoracic pain was grade 3 and cardiac insufficiency was grade 2.

The investigator considered the events were not related to study drug or to concomitant treatments.

Follow-up (03Jul2023): This is a follow-up from a non-interventional study report received from the investigator via the CRO.
Updated information included: updated patient's height.

Case Comment: In agreement with the reporter, the Company considers that the possibility that the suspect drug bosutinib may have caused the reported events chest pain and cardiac failure can be excluded.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	17-MAY-2021	Angiocardiogram and right coronary 50%	stenosis of interior intraventricular artery 2=40%	

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	FRANCE		PRIVACY		45 Years	Female	95.00 kg	14	APR	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

POSITIONAL MYALGIA [Myalgia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200098625

24c. DATE RECEIVED BY MANUFACTURER
06-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200098625

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 45-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), (ongoing). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: MYALGIA (non-serious) with onset 14Apr2020, outcome "recovered" (2020), described as "POSITIONAL MYALGIA". The action taken for bosutinib was dosage not changed.

The reporter considered "positional myalgia" not related to bosutinib.

Additional information: Two events were assessed as non-serious and rated grade 1.

Follow-up attempts are completed. No further information is expected.

Amendment:This follow-up report is being submitted to amend previously reported information: The patient's gender was updated to female.

Follow-up (06Sep2023): This is a follow-up report from the investigator via CRO. New information received included: The event anxiety was removed.

No Follow-up attempts are needed. No further information is expected.

Case Comment: The event "positional myalgia" is an intercurrent medical condition, not related to the suspect drug bosutinib.

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	FRANCE		PRIVACY		67 Years	Female	74.00 kg	08	AUG	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Martial deficiency [Iron deficiency]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 16-DEC-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)

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200101901

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since 16Dec2016 (ongoing) at 300 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: IRON DEFICIENCY (non-serious) with onset 08Aug2019, outcome "not recovered", described as "Martial deficiency". The action taken for bosutinib was dosage not changed.

The reporter considered "martial deficiency" not related to bosutinib.
Additional information: Iron deficiency rated grade 2, non-serious. The event was unrelated to bosutinib and to any concomitant drug. The site reported: "known recurrent martial deficiency".

No follow-up attempts are possible. No further information is expected.

Case Comment: The event Iron deficiency was attributed to an intercurrent medical condition and unrelated to bosutinib.

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	FRANCE		PRIVACY		76 Years	Male	76.30 kg	05	NOV	2020

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
Arthrosis flare-up (grade 4) [Osteoarthritis]
DIARRHEA [Diarrhoea]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) NILOTINIB (NILOTINIB)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK	#1) Unknown
#2) UNK	#2) Unknown

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) 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
Unknown		

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200110342

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

B1871047.

A 76-year-old male patient received bosutinib (BOSULIF); nilotinib (NILOTINIB), (Batch/Lot number: unknown). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DIARRHOEA (non-serious) with onset 05Nov2020, outcome "recovered" (04Feb2021), described as "DIARRHEA"; OSTEOARTHRITIS (hospitalization, medically significant) with onset 27Feb2021, outcome "recovered" (Feb2021), described as "Arthrosis flare-up (grade 4)". The action taken for bosutinib and nilotinib was dosage not changed.

The reporter considered "arthrosis flare-up (grade 4)" not related to bosutinib. The reporter considered "diarrhea" related to bosutinib.

Additional information: According to the investigator, the events were unrelated to concomitant medications.

Follow-up (05Jul2022): This is a non-interventional study follow up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047. Updated information: new event (diarrhea).

Follow-up (18Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information includes: event diarrhea was resolved on 04Feb2021.

Case Comment: There was not a reasonable possibility that the event "arthrosis flare-up (grade 4)" was related to suspect drug, bosutinib and is most likely due to the underlying disease of osteoarthritis. Based on the known drug safety profile, a causal association between bosutinib and the event diarrhea cannot be excluded. This case will be reassessed when further information is provided.

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	FRANCE		PRIVACY		64 Years	Female	111.00 kg	26	DEC	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

left eyelid lesion [Eyelid disorder]
right iliac fossa pain [Abdominal pain lower]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 100 mg, 1x/day

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) 12-NOV-2018 / 18-NOV-2018

19. THERAPY DURATION
#1) 7 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200111284

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
06-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200111284

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 64-year-old female patient received bosutinib (BOSULIF), first regimen from 12Nov2018 to 18Nov2018 at 100 mg 1x/day, second regimen from 19Nov2018 to 25Nov2018 at 200 mg 1x/day, third regimen from 26Nov2018 to 02Dec2018 at 300 mg 1x/day and fourth regimen since 03Dec2018 (ongoing) at 400 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: EYELID DISORDER (non-serious) with onset 26Dec2019, outcome "recovered" (2020), described as "left eyelid lesion"; ABDOMINAL PAIN LOWER (non-serious) with onset 2021, outcome "recovered" (May2021), described as "right iliac fossa pain". The action taken for bosutinib was dosage not changed.

The reporter considered "left eyelid lesion" and "right iliac fossa pain" not related to bosutinib.

Additional information: Left eyelid lesion was rated grade 1. Right iliac fossa pain was rated grade 2.

No follow-up attempts are possible. No further information is expected.

Follow-up (15May2023): This is a non-interventional study follow-up report received from contactable reporter(s) (Other HCP) for protocol B1871047.
Updated information: new reporter (Other HCP).

Follow-up (06Sep2023): This is a non-interventional study follow-up report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

Updated information includes: bosutinib therapy dates and regimens.

Case Comment: Events left eyelid lesion and right iliac fossa pain are most likely related to intercurrent or underlying conditions and unrelated to study drug BOSUTINIB.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, 1x/day; Unknown	Unknown	19-NOV-2018 / 25-NOV-2018; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, 1x/day; Unknown	Unknown	26-NOV-2018 / 02-DEC-2018; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg, 1x/day; Unknown	Unknown	03-DEC-2018 / Ongoing; Unknown

CIOMS FORM

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	FRANCE		PRIVACY		77 Years	Male	76.30 kg	20	NOV	2021	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Basedow's disease [Graves' disease]
RAPID ATRIAL FIBRILLATION [Atrial fibrillation]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
(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 mg	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 10-NOV-2019 / 16-NOV-2019	#1) 7 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NILOTINIB (NILOTINIB) ; 04-FEB-2021 / 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	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200111465

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 77-year-old male patient received bosutinib (BOSULIF), first regimen from 10Nov2019 to 16Nov2019 at 100 mg, second regimen from 17Nov2019 to 23Nov2019 at 200 mg, third regimen from 24Nov2019 to 18Jan2020 at 300 mg and fourth regimen from 19Jan2020 to 16Jan2021 at 400 mg daily. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: NILOTINIB oral taken for chronic myeloid leukaemia, start date: 04Feb2021 (ongoing). The following information was reported: GRAVES' DISEASE (non-serious) with onset 20Nov2021, outcome "not recovered", described as "Basedow's disease"; ATRIAL FIBRILLATION (non-serious) with onset 02Dec2021, outcome "not recovered", described as "RAPID ATRIAL FIBRILLATION". Relevant laboratory tests and procedures are available in the appropriate section. Therapeutic measures were taken as a result of graves' disease.

The reporter considered "basedow's disease" and "rapid atrial fibrillation" not related to bosutinib.

Additional information: The patient then switched to Nilotinib from 04Feb2021 and ongoing. Both events occurred several months after Bosulif was stopped. For Basedow's disease, confirmation of diagnosis on 08Dec2021 associated symptomatology: loss of 8 kgs, tachycardia, quick reflexes, dyspnea on effort, lower TSH, increase in T4; treated by thiamazole (THYROZOL) from 17Dec2021. The event Basedow's disease was rated grade 2. Event reported as non-serious. The event Atrial fibrillation was rated grade 2. Event reported as non-serious. The investigator considered that the event was unrelated to study drug or to any concomitant drug.

Follow-up attempts are completed. No further information is expected.

Follow-up (07Sep2022): This is a non-interventional study follow up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: lab data, new events (Basedow's disease and atrial fibrillation).

Follow-up (20Sep2022): This is a non-interventional study follow up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: dyspnea and tachycardia are symptoms of Basedow's disease and therefore removed

Follow-up (18Jul2023): This is a non-interventional study follow up report received from the investigational site via the CRO. Updated information includes: Event RAPID ATRIAL FIBRILLATION onset date was changed to 02Dec2021.

Follow-up (07Sep2023 and 07Sep2023): This is a non-interventional study follow up report received from the clinical team in response to query and investigational site via CRO.
Updated information includes: medical history added, dosage regimen, action taken of bosutinib added and Nilotinib information.

Case Comment: Based on "the patient switched to Nilotinib from 04Feb2021 and ongoing. Both events occurred several months after Bosulif was stopped", the Company concurs with the investigator that there is not a reasonable possibility that the events, Basedow's disease and atrial fibrillation, were related to bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	08-DEC-2021	Blood thyroid stimulating hormone	lower	
2	08-DEC-2021	Thyroxine	increase	
3	08-DEC-2021	Weight	loss of 8 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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg; Unknown	Unknown	17-NOV-2019 / 23-NOV-2019; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg; Unknown	Unknown	24-NOV-2019 / 18-JAN-2020;

Mfr. Control Number: 202200111465

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 month 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg, daily; Unknown	Unknown	19-JAN-2020 / 16-JAN-2021; 11 months 29 days

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	FRANCE		PRIVACY		66 Years	Female	111.00 kg	10	DEC	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

VARICOSITIES OF THE LOWER LIMBS [Varicose vein]
EROSION OF THE BUCCAL MUCOSA [Oral mucosa erosion]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200111480

24c. DATE RECEIVED BY MANUFACTURER
29-JUN-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 66-year-old female patient received bosutinib (BOSULIF), (ongoing). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ORAL MUCOSA EROSION (non-serious) with onset 10Dec2020, outcome "recovered" (Dec2020), described as "EROSION OF THE BUCCAL MUCOSA"; VARICOSE VEIN (non-serious) with onset 09Dec2021, outcome "not recovered", described as "VARICOSITIES OF THE LOWER LIMBS". The action taken for bosutinib was dosage not changed.

The reporter considered "varicosities of the lower limbs" and "erosion of the buccal mucosa" not related to bosutinib.

Additional information: Both events were grade 1, unrelated to study drug or concomitants.
No follow-up attempts are possible. No further information is expected.

Amendment: This follow-up report is being submitted to amend previously reported information: the patient was a female subject.

Case Comment: Based on the information provided, there is not a reasonable possibility that the events "varicosities of the lower limbs" and "erosion of the buccal mucosa" were related to bosutinib. Of note, the event "erosion of the buccal mucosa" resolved while treatment with bosutinib was ongoing without any change.

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	FRANCE		PRIVACY		76 Years	Male	76.00 kg	13	JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

DYSPNEA [Dyspnoea]
PLEURAL EFFUSION [Pleural effusion]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
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New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200114267

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
18-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 76-year-old male patient received bosutinib (BOSULIF). The patient's relevant medical history and concomitant medications were not reported. The following information was reported: DYSPNOEA (hospitalization) with onset 13Jun2020, outcome "recovered" (Sep2020), described as "DYSPNEA"; PLEURAL EFFUSION (non-serious) with onset 13Jul2020, outcome "recovered" (14Oct2020). The events dyspnea and pleural effusion were reported as grade 2. The action taken for bosutinib was dosage permanently withdrawn.

The investigator considered there was not a reasonable possibility that the event 'dyspnea' was related to bosutinib. The investigator considered there was a reasonable possibility that the event 'pleural effusion' was related to bosutinib.

No follow-up attempts are needed. No further information is expected.

Follow-up (05Jul2022): This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047 (Study alias BOSEVAL). Updated information includes: onset date of the event "Dyspnea" updated from 13Jul2020 to 13Jun2020.

Follow-up (18Jul2023): This is follow-up non-interventional study report received from the investigational site via CRO.
Updated information includes: stop date of event Pleural effusion updated to 14Oct2020.

No follow-up attempts are needed. No further information is expected.

Case Comment: In agreement with the reporter, the Company considers the reported event dyspnoea as unrelated to the administration of bosutinib; conversely,the adverse event pleural effusion is considered related to bosutinib.
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
PRIVACY	FRANCE		PRIVACY		76 Years	Male	76.30 kg	15	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pleural effusion [Pleural effusion]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 24-OCT-2020 / 16-JAN-2021

19. THERAPY DURATION
#1) 2 months 24 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200116528

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
19-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 76-year-old male patient received bosutinib (BOSULIF), from 24Oct2020 to 16Jan2021 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: PLEURAL EFFUSION (non-serious) with onset 15Jan2021, outcome "recovered" (04Feb2021). The action taken for bosutinib was temporarily withdrawn on 16Jan2021. Rechallenge of bosutinib was performed and "pleural effusion" reoccurred.

The reporter considered "pleural effusion" related to bosutinib.

Additional information: Event was grade 2. Study drug was temporarily withdrawn on 16Jan2021. Event recurred after the treatment was resumed. According to the investigator event was unrelated to concomitant treatments.

Case Comment: Based on available information, a possible contributory role of the subject drug BOSUTINIB cannot be excluded for the reported event Pleural effusion.

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	FRANCE		PRIVACY		75 Years	Male	76.30 kg	14	NOV	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Diarrhea grade 1 [Diarrhoea]
Pharyngitis grade 1 [Pharyngitis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 10-NOV-2019 / 16-NOV-2019	#1) 7 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) XARELTO (RIVAROXABAN) ; DEC-2014 / Ongoing
#2) IRBESARTAN (IRBESARTAN) ; 2011 / Ongoing

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 Ongoing	Relevant Med History	Arterial hypertension (Hypertension)
DEC-2014 to Ongoing	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
	cardiac arrhythmia by atrial fibrillation	

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200116794

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
05-JUL-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), first regimen from 10Nov2019 to 16Nov2019 at 100 mg daily, second regimen from 17Nov2019 to 23Nov2019 at 200 mg daily, third regimen from 24Nov2019 to 18Jan2020 at 300 mg daily and fourth regimen since 19Jan2020 (ongoing) at 400 mg daily. The patient's relevant medical history included: "ARTERIAL HYPERTENSION", start date: 2011 (ongoing); "cardiac arrhythmia by atrial fibrillation", start date: Dec2014 (ongoing), notes: cardiac arrhythmia by atrial fibrillation. Concomitant medication(s) included: XARELTO oral taken for atrial fibrillation, start date: Dec2014 (ongoing); IRBESARTAN oral taken for hypertension, start date: 2011 (ongoing).
The following information was reported: DIARRHOEA (non-serious) with onset 14Nov2019, outcome "recovered" (2020), described as "Diarrhea grade 1"; PHARYNGITIS (non-serious) with onset 29Nov2019, outcome "recovered" (Dec2019), described as "Pharyngitis grade 1". The action taken for bosutinib was dosage not changed.

The reporter considered "diarrhea grade 1" related to bosutinib. The reporter considered "pharyngitis grade 1" not related to bosutinib. Additional information: The events were unrelated to any concomitant drugs.

No follow-up attempts are possible. No further information is expected.

Follow-up (05Jul2022): This is a non- interventional study follow up report for protocol B1871047 received from investigational site via CRO.

Updated information: outcome of event diarrhea updated to recovered and recovery date provided.

Case Comment: Based on the information provided and known safety profile, there is a reasonable possibility that the reported diarrhea is related to bosutinib. The reported pharyngitis is likely an intercurrent medical condition and unrelated to bosutinib.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, daily; Unknown	Unknown	17-NOV-2019 / 23-NOV-2019; 7 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, daily; Unknown	Unknown	24-NOV-2019 / 18-JAN-2020; 1 month 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg, daily; Unknown	Unknown	19-JAN-2020 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		65 Years	Male	95.00 kg			2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

UPPER AIRWAY INFECTION EPISODE [Upper respiratory tract infection]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(Continued on Additional Information Page)

15. DAILY DOSE(S)
#1) 300 mg

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 04-JUN-2018 / 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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200148764

24c. DATE RECEIVED BY MANUFACTURER
21-APR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200148764

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 65-year-old male patient received bosutinib (BOSULIF), first regimen since 04Jun2018 at 300 mg and second regimen till 19Feb2020. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: UPPER RESPIRATORY TRACT INFECTION (non-serious) with onset 2019, outcome "recovered" (2019), described as "UPPER AIRWAY INFECTION EPISODE". The action taken for bosutinib was dosage permanently withdrawn on 19Feb2020.

Additional information: Event was grade 2. It was reported that the last dosage before the onset of the event was 300 mg from 04Jun2018, bosutinib was ongoing when the event occurred. Bosutinib was permanently withdrawn on 19Feb2020.

The reporter considered "upper airway infection episode" not related to bosutinib.

Follow-up (13Apr2023): New information received from investigational site via CRO. Updated information included: patient's date of birth. Patient's age was added.

Follow-up (21Apr2023): New information received from the clinical team.
Updated information included: suspect drug dosage regimen and action taken.

Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the information provided, the event upper respiratory tract infection is most likely attributed to an intercurrent medical condition and unrelated to bosutinib. Of note, the event outcome was recovered but the action taken for bosutinib was dosage not changed.
The follow up information does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	UNK; Unknown	Unknown	Unknown / 19-FEB-2020; 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
PRIVACY	FRANCE		PRIVACY		72 Years	Male	68.00 kg	10	JUN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

OEDEMA OF THE LOWER LIMBS [Oedema peripheral]
INTESTINAL POLYPS [Intestinal polyp]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 20-SEP-2018 / 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
2002 to 2018	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
2014 to 2014	Relevant Med History	Stroke (Cerebrovascular accident)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200153749

24c. DATE RECEIVED BY MANUFACTURER
26-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200153749

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 72 year-old male patient received bosutinib (BOSULIF), since 20Sep2018 (ongoing) (Batch/Lot number: unknown) at 400 mg daily. Relevant medical history included: "Cardiac arrhythmia due to atrial fibrillation", start date: 2002, stop date: 2018; "stroke", start date: 2014, stop date: 2014. The patient's concomitant medications were not reported.
The following information was reported: OEDEMA PERIPHERAL (non-serious) with onset 10Jun2021, outcome "recovered" (Jun2021), described as "OEDEMA OF THE LOWER LIMBS"; INTESTINAL POLYP (non-serious) with onset 2021, outcome "recovered" (20May2021), described as "INTESTINAL POLYPS". The action taken for bosutinib was dosage not changed.

The investigator considered there was not a reasonable possibility that the events "oedema of the lower limbs" and "intestinal polyps" were related to bosutinib.

Additional information: the events were grade 2, non-serious, unrelated to bosutinib or to any concomitant drug.

No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the available information, the company concurs with the reporting investigator that there was not a reasonable possibility that the events "oedema of the lower limbs" and "intestinal polyps" were related to bosutinib. The underlying cardiovascular and history of stroke may have played an important contributory role to the 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
PRIVACY	FRANCE		PRIVACY		72 Years	Male	68.00 kg	19	MAY	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

IRON DEFICIENCY ANEMIA grade 3 [Iron deficiency anaemia]
ANGIODYSPLASIA OF THE COLON grade 2 [Gastrointestinal angiodysplasia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 20-SEP-2018 / 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
2002 to 2018	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
2014 to 2014	Relevant Med History	Stroke (Cerebrovascular accident)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200154868

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 72 year-old male patient received bosutinib (BOSULIF), since 20Sep2018 (ongoing) (Batch/Lot number: unknown) at 400 mg daily. Relevant medical history included: "cardiac arrhythmia due to atrial fibrillation", start date: 2002, stop date: 2018; "STROKE", start date: 2014, stop date: 2014. The patient's concomitant medications were not reported.
The following information was reported: IRON DEFICIENCY ANAEMIA (hospitalization) with onset 19May2021, outcome "recovered" (21May2021), described as "IRON DEFICIENCY ANEMIA grade 3"; GASTROINTESTINAL ANGIODYSPLASIA (non-serious) with onset 20May2021, outcome "recovered" (26Jul2021), described as "ANGIODYSPLASIA OF THE COLON grade 2". The patient was hospitalized for iron deficiency anaemia (start date: 19May2021, discharge date: 21May2021, hospitalization duration: 2 day(s)). The action taken for bosutinib was dosage not changed.

Additional information: The patient was hospitalized for upper endoscopy and colonoscopy following persistent iron deficiency anemia from 19May2021 to 21May2021.

The investigator considered there was not a reasonable possibility that the events "iron deficiency anemia grade 3" and "angiodysplasia of the colon grade 2" were related to bosutinib nor any concomitant drug.

No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the available information, the Company concurs with the investigator that there is not a reasonable possibility that the events "iron deficiency anemia grade 3" and "angiodysplasia of the colon grade 2" are related to bosutinib. The events are more likely inter-current medical conditions.

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	FRANCE		PRIVACY		71 Years	Male	68.00 kg	19	FEB	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Iron deficiency anemia [Iron deficiency anaemia]
Iron deficiency anemia [Iron deficiency anaemia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report for protocol B1871047.

A 71 year-old male patient received bosutinib (BOSULIF), since

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 20-SEP-2018 / 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
2002 to 2018	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
2014 to 2014	Relevant Med History	Stroke (Cerebrovascular accident)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200155090

24c. DATE RECEIVED BY MANUFACTURER
26-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

20Sep2018 (ongoing) (Batch/Lot number: unknown) at 400 mg daily. Relevant medical history included: "Atrial fibrillation", start date: 2002, stop date: 2018; "Stroke", start date: 2014, stop date: 2014. The patient's concomitant medications were not reported.
The following information was reported: IRON DEFICIENCY ANAEMIA (hospitalization) with onset 19Feb2021, outcome "recovered" (22Feb2021), IRON DEFICIENCY ANAEMIA (hospitalization) with onset 15Jun2021, outcome "recovered" (29Jun2021) and all described as "Iron deficiency anemia". Both events were rated as grade 3. The action taken for bosutinib was dosage not changed.

The investigator considered there was not a reasonable possibility that the event "iron deficiency anemia" was related to bosutinib nor concomitant drug.

No follow-up attempts are possible. No further information is expected.

Case Comment: Both episodes of Iron deficiency anemia are deemed unrelated to the study drug, bosutinib.

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	FRANCE		PRIVACY		71 Years	Male	68.00 kg		FEB	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Gastritis burn [Reflux gastritis]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 20-SEP-2018 / 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
2002 to 2018	Relevant Med History	Atrial fibrillation (Atrial fibrillation)
2014 to 2014	Relevant Med History	CVA (Cerebrovascular accident)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200168495

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
26-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200168495

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 71-year-old male patient received bosutinib (BOSUTINIB), since 20Sep2018 (ongoing) at 400 mg daily. The patient's relevant medical history included: "Atrial fibrillation", start date: 2002, stop date: 2018; "CVA (Cerebrovascular accident)", start date: 2014, stop date: 2014. The patient's concomitant medications were not reported.
The following information was reported: REFLUX GASTRITIS (non-serious) with onset Feb2021, outcome "recovering", described as "Gastritis burn". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.
The reporter considered "gastritis burn" not related to bosutinib.

Additional information: Gastritis burn, grade 2, non-serious, unrelated to the study drug or concomitant medications. Ulcerative gastritis showed in fibroscopy on 20May2021.

No follow-up attempts are needed. No further information is expected.

Case Comment: Based on the information provided, the event Gastritis burn is assessed as unrelated to bosutinib. There is no known association between the event and the drug. Of note, the outcome of the event is recovering and the action taken for bosutinib was dosage not changed. The case will be re-evaluated if more information is available.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	20-MAY-2021	Endoscopy	Ulcerative 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	FRANCE		PRIVACY		71 Years	Female	Unk	27	MAY	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Anxiety [Anxiety]
Scalp pruritus [Pruritus]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic Myeloid Leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 18-MAR-2019 / 30-APR-2019

19. THERAPY DURATION
#1) 1 month 13 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) TASIGNA (NILOTINIB HYDROCHLORIDE) ; 27-MAY-2019 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200172556

24c. DATE RECEIVED BY MANUFACTURER
16-MAY-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 71-year-old female patient received bosutinib (BOSULIF), from 18Mar2019 to 30Apr2019 at 400 mg daily for chronic myeloid leukaemia. The patient's relevant medical history was not reported. Concomitant medication(s) included: TASIGNA oral taken for chronic myeloid leukaemia, start date: 27May2019 (ongoing).
The following information was reported: ANXIETY (non-serious) with onset 27May2019, outcome "recovered" (29Jun2019); PRURITUS (non-serious) with onset 11Jun2019, outcome "not recovered", described as "Scalp pruritus".

Additional information: Anxiety and Itchy scalp were reported as non-serious with grade 1. Action taken for event Anxiety was reported as not applicable for Bosulif and dose not changed for Tasigna. Action taken for event Itchy scalp was reported as Dose reduced for Tasigna.

According to the investigator, the events anxiety and Itchy scalp were unrelated to study drug and unrelated to concomitant drugs.

No follow-up attempts are need. No further information is expected.

Follow-up (16May2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047. Updated information includes: added concomitant drug TASIGNA, added event Itchy scalp.

Case Comment: Event ANXIETY represents an intercurrent medical condition and unrelated to bosutinib. Based on available information and known safety profile of the suspect product the reasonable possibility that bosutinib played a contributory role toward the reported itchy scalp 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
PRIVACY	FRANCE		PRIVACY		58 Years	Male	70.00 kg	01	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Urinary tract infection [Urinary tract infection]
Urinary tract infection [Urinary tract infection]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 22-JAN-2019 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200172972

24c. DATE RECEIVED BY MANUFACTURER
20-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200172972

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 58-year-old male patient received bosutinib (BOSULIF), since 22Jan2019 (ongoing) at 400 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history and concomitant medications were not reported. The following information was reported: URINARY TRACT INFECTION (non-serious) with onset 01Jan2021, outcome "recovered" (14Jan2021), URINARY TRACT INFECTION (non-serious) with onset 16Aug2021, outcome "recovered" (Mar2022) and all described as "Urinary tract infection". The action taken for bosutinib was dosage not changed.
Additional information: urinary tract infection grade 2 and recovered, unrelated to study drug or concomitant.
According to the investigator, the event was non-serious and not related to study drug or concomitant medication.

No follow-up attempts are needed. No further information is expected.

Follow-up (28Jul2022): This is a follow-up report from an investigational site via CRO. Updated information: clinical course of events.

Follow-up(23Feb2023): New information received from investigational site via CRO included: second epidose of urinary infection from 16Aug2021 to Mar2022, unreated to treatment, non-serious, grade 2, dose of bosulif not changed in response to the event

Follow-up (20Jul2023 and 21Jul2023): This is a follow-up report from an investigational site via CRO. Updated information: Onset of bosulif changed to 22Jan2019.

Case Comment: The reported two episodes of urinary tract infection likely represent intercurrent medical conditions and are considered unrelated to bosutinib.

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	FRANCE		PRIVACY		35 Years	Female	59.00 kg	20	JUN	2019	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Night sweats [Night sweats]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 05-MAR-2019 / 20-JUN-2019

19. THERAPY DURATION
#1) 3 months 16 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200173959

24c. DATE RECEIVED BY MANUFACTURER
16-MAY-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 35-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 05Mar2019 to 20Jun2019 at 400 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: NIGHT SWEATS (non-serious) with onset 20Jun2019, outcome "recovered" (02Sep2021).
The action taken for bosutinib was dosage not changed.

The reporter considered "night sweats" not related to bosutinib.

Additional information: The event was grade 2, non-serious. As per the investigator, the event was unrelated to study drug and concomitant treatments.

No follow-up attempts are needed. No further information is expected.

Follow-up (16May2023): This is a follow-up report received from the CRO. Updated information included: The event's grade was changed from grade 1 to grade 2.

Case Comment: Event night sweats represents an intercurrent medical condition and unrelated to bosutinib .

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	FRANCE		PRIVACY		65 Years	Male	95.00 kg		DEC	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Rhinopharyngitis [Nasopharyngitis]
Flu [Influenza]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 04-JUN-2018 / 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) VALSARTAN (VALSARTAN) ; 2005 / Ongoing
#2) BISOPROLOL (BISOPROLOL) ; 2005 / Ongoing
#3) ROSUVASTATIN (ROSUVASTATIN) ; 2005 / 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	Ischemic cardiomyopathy (Ischaemic cardiomyopathy)
Unknown to Ongoing	Relevant Med History	Gastritis (Gastritis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200176288

24c. DATE RECEIVED BY MANUFACTURER
13-APR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200176288

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 65-year-old male patient received bosutinib (BOSULIF), since 04Jun2018 (ongoing) at 300 mg daily. The patient's relevant medical history included: "Ischemic cardiomyopathy" (ongoing); "GASTRITIS" (ongoing). Concomitant medication(s) included: VALSARTAN oral taken for ischaemic cardiomyopathy, start date: 2005 (ongoing); BISOPROLOL oral, start date: 2005 (ongoing); ROSUVASTATIN oral, start date: 2005 (ongoing).
The following information was reported: NASOPHARYNGITIS (non-serious) with onset Dec2019, outcome "recovered" (Dec2019), described as "Rhinopharyngitis"; INFLUENZA (non-serious) with onset 2020, outcome "recovered" (2020), described as "Flu". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.

The reporter considered "rhinopharyngitis" and "flu" not related to bosutinib.

Additional information: The events "rhinopharyngitis" and "flu" were rated non-serious with grade 1. According to the investigator, both events were unrelated to the study drug bosutinib and unrelated to concomitant drugs.

Follow-up (13Apr2023): This is a follow-up report received from the CRO.
Updated information included: Reporter information, bosutinib start date.

Case Comment: Based on the information provided, the events "rhinopharyngitis" and "flu" are more likely attributed to intercurrent medical conditions and unrelated to bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-APR-2018	Endoscopy upper gastrointestinal tract	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	FRANCE		PRIVACY		69 Years	Female	58.00 kg		OCT	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Cough [Cough]
Anorexia [Decreased appetite]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 24-FEB-2016 / 03-MAR-2016

19. THERAPY DURATION
#1) 9 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200178643

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
31-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 69-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 24Feb2016 to 03Mar2016 at 300 mg daily.
The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DECREASED APPETITE (non-serious) with onset Oct2016, outcome "not recovered", described as "Anorexia"; COUGH (non-serious) with onset Oct2016, outcome "recovered" (Oct2016). The action taken for bosutinib was unknown.

The reporter considered "cough" and "anorexia" not related to bosutinib.

Additional information: The events cough and anorexia were reported as non-serious with grade 1. According to the investigator, the events were unrelated to study drug and unrelated to concomitant drugs.
No follow-up attempts are needed. No further information is expected.

Case Comment: The Company agrees with the assessment of the investigator and reasonably does not attribute the events to study drugs and concomitant drugs. Events are likely intercurrent medical conditions associated with the underlying malignancy.

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	FRANCE		PRIVACY		68 Years	Female	58.00 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)

Nocturnal pollakiuria (grade 1) [Pollakiuria]
Burning mouth (grade 1) [Oral discomfort]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 23-FEB-2016 / 01-MAR-2016

19. THERAPY DURATION
#1) 8 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	Arterial hypertension (Hypertension)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200178772

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
31-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200178772

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 68-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 23Feb2016 to 01Mar2016 at 300 mg daily. The patient's relevant medical history included: "Arterial hypertension" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: POLLAKIURIA (non-serious) with onset 04Apr2016, outcome "recovered" (05Apr2016), described as "Nocturnal pollakiuria (grade 1)"; ORAL DISCOMFORT (non-serious) with onset 06Oct2016, outcome "recovered" (Oct2016), described as "Burning mouth (grade 1)".

The reporter considered "nocturnal pollakiuria (grade 1)" and "burning mouth (grade 1)" not related to bosutinib.

Additional information: The events nocturnal pollakiuria and burning mouth were reported as non-serious grade 1. According to the investigator, the events were unrelated to study drug and unrelated to concomitant drugs.

No follow-up attempts are needed. No further information is expected.

Case Comment: Based on the available information, the Company considers both events are unrelated to suspect drug bosutinib but more likely inter-current medical conditions.

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	FRANCE		PRIVACY		Unk	Female	Unk	02	SEP	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
Cervicalgia [Neck pain]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200179047

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-JAN-2022

24d. REPORT SOURCE
- ☒ STUDY
- ☐ LITERATURE
- ☒ HEALTH PROFESSIONAL
- ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
- ☒ INITIAL
- ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A female patient (unknown if pregnant) received bosutinib (BOSUTINIB) (Batch/Lot number: unknown). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: NECK PAIN (medically significant) with onset 02Sep2019, outcome "unknown", described as "Cervicalgia". It was described as that on 02Sep2019 asthenia, nausea, episodes of malaise related to a cervical discomfort. On 24Sep2019, she went to the emergency room for headache, fever, neck pain, dizziness, vomiting, nausea and was finally diagnosed with cervicalgia. The action taken for bosutinib was unknown. The patient discontinued bosutinib due to unspecified reason and was treated with nilotinib hydrochloride (TASIGNA) from an unspecified date.

The reporter's assessment of the causal relationship of the "cervicalgia" with the suspect product(s) bosutinib 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: The event Cervicalgia is serious and unrelated to the suspect drug, bosutinib (BOSUTINIB). This case will be reassessed when further information is provided.

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	FRANCE		PRIVACY		69 Years	Female	58.00 kg	14	DEC	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

LEFT LOWER LIMB ARTERIAL ULCER [Skin ulcer]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

A 69 year-old female patient received bosutinib (BOSULIF), from

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 24-FEB-2016 / 03-MAR-2016

19. THERAPY DURATION
#1) 9 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200188073

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

24Feb2016 (Batch/Lot number: unknown) to 03Mar2016 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: SKIN ULCER (hospitalization) with onset 14Dec2016, outcome "not recovered", described as "LEFT LOWER LIMB ARTERIAL ULCER". The patient was hospitalized for skin ulcer (start date: 14Dec2016, discharge date: 23Dec2016, hospitalization duration: 9 day(s)).

The investigator considered there was not a reasonable possibility that the event "left lower limb arterial ulcer" was related to bosutinib.
Additional information: The event left lower limb arterial ulcer was rated serious with grade 3.

No follow-up attempts are possible. No further information is expected.

Follow-up (07Feb2022): This is a non-interventional study follow up report (Post Authorization Safety Study) for protocol B1871047 received from study site via CRO.

Updated information: Event grade was updated to grade 3.

Case Comment: There is not a reasonable possibility that the event LEFT LOWER LIMB ARTERIAL ULCER was related to bosutinib. The onset of the event was 9-month post therapy.

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	FRANCE		PRIVACY		68 Years	Female	58.00 kg		OCT	2016

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

DRY MOUTH [Dry mouth]
DYSPNEA [Dyspnoea]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE.

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 24-FEB-2016 / 03-MAR-2016

19. THERAPY DURATION
#1) 9 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200188354

24c. DATE RECEIVED BY MANUFACTURER
31-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 68-year-old female patient received bosutinib (BOSULIF), from 24Feb2016 to 03Mar2016 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DRY MOUTH (non-serious) with onset Oct2016, outcome "recovered" (Oct2016); DYSPNOEA (non-serious) with onset Oct2016, outcome "recovered" (Nov2016), described as "DYSPNEA". The action taken for bosutinib was dosage not changed.

The reporter considered "dry mouth" and "dyspnea" not related to bosutinib.

Additional information: Both events were rated non-serious with grade 1.
The action taken in response to both events for the study drug bosutinib was dosage not changed. According to the investigator both events were unrelated to the study drug bosutinib and unrelated to concomitant drug.

No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the information provided, there is no temporal relationship between the events dyspnea and dry mouth and the administration of bosutinib. Events occurred 7 months after the last dose of bosutinib. Events are likely intercurrent medical condition in this 68-year-old female patient.

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	FRANCE		PRIVACY		69 Years	Male	86.00 kg		MAR	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Rectorrhagia [Rectal haemorrhage]
Hiatal hernia [Hiatus hernia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 400 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 15-JAN-2019 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200193649

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
16-MAR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200193649

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 69-year-old male patient received bosutinib (BOSULIF), since 15Jan2019 (ongoing) at 400 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: RECTAL HAEMORRHAGE (non-serious) with onset Mar2021, outcome 'recovered' (2021), described as 'Rectorrhagia'; HIATUS HERNIA (non-serious) with onset Jun2021, outcome 'not recovered', described as 'Hiatal hernia'. Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.

The reporter considered 'rectorrhagia' and 'hiatal hernia' not related to bosutinib.

Additional information: Additional information: during the consultation of 08Mar2021 and 15Sep2021, blood in stool was reported . During the consultation of 07Jun2021, it was noted subject underwent digestive examinations revealing hiatal hernia and coloscopy revealing a lesion of bottom low caecal which was bleeding. Both rectorrhagia and Hiatal hernia were grade 1 assessed as non-serious. Lesion of bottom low caecal was not reported as adverse event.

Follow-up (07Feb2022). This a non-interventional study follow-up report from the investigational site via CRO.
Updated information: patient's demographics, bosutinib dosage details updated, and deleted event 'Lesion of bottom low caecal which was bleeding', reporter causality Added

Follow-up (16Mar2023): This a non-interventional study follow-up report from clinical team.
Update information includes: lesion of bottom low caecal from 08Mar2021 to Sep2021 (not reported as adverse event in the E-CRF)

Case Comment: The events grade 1 'rectorrhagia' and 'hiatal hernia' which was bleeding are assessed as unrelated to bosutinib. Details regarding the drug-event temporal relationship, clinical course of the events, patient's medical history and concomitant medications are not reported. The case will be re-evaluated if more information is available.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Colonoscopy	lesion of bottom low caecal which was bleeding	
2		Gastrointestinal examination hiatal hernia	hiatal hernia	

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	FRANCE		PRIVACY		68 Years	Male	103.00 kg	16	OCT	2020

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
Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy of 26Mar2021) [Second primary malignancy]
Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy of 26Mar2021) [Gastrointestinal stromal tumour]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic lymphoid leukemia (Chronic lymphocytic leukaemia)

18. THERAPY DATES(from/to)
#1) 14-DEC-2017 / 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	Relevant Med History	Adenoma (Adenoma benign)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200194074

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-MAR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable Physician for protocol B1871047.

A 68-year-old male subject received bosutinib (BOSUTINIB), since 14Dec2017 (ongoing) at 500 mg daily for chronic lymphoid leukemia. The patient's relevant medical history included: "adenomatous polyps" (unspecified if ongoing). The subject's concomitant medications were not reported.
The following information was reported: SECOND PRIMARY MALIGNANCY (medically significant), GASTROINTESTINAL STROMAL TUMOUR (medically significant) all with onset 16Oct2020, outcome "recovered" (Jul2021) and all described as "Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy of 26Mar2021)". Gastroscopy was performed on 16Oct2020 showing a big sub-mucosal gastric nodule, which increased of size. On 05Feb2021, high echo endoscopy was performed and showed sub-mucosal tumour of 5 cm of the fourth layer hypoechogenous evoking a gastrointestinal stromal tumor. The finding date of the gastric nodule was on 26Mar2021, date on which the biopsy was performed, whether 28 days after the visit M36, not considered as an adverse event according to protocol. Surgery with removal of the gastrointestinal stromal tumor was performed on 15Jul2021, then gastric decompensation at the end of Jul2021 and favorable outcome. The event Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy of 26Mar2021) was reported as serious (medically significant) with grade 3. The action taken for bosutinib was dosage not changed.

According to the investigator, the event was unrelated to study drug bosutinib and unrelated to concomitant drugs.

Follow-up (21Mar2022 and 28Mar2022): New information received from the investigational site investigator via the CRO. Updated information: patient details (date of birth, height, and weight), medical history, lab data, event details (onset and stop date), reaction data (new event: Condition aggravated was added) outcome of event, causality and seriousness. This case was upgraded to serious.

Follow-up (16May2022): This is a non-interventional study follow-up report received from the investigational site via CRO.
Updated information includes: study drug dosage regimen and therapy date.

Follow-up (27Jun2022): new information received from the investigational site.
Updated information: Bosutinib indication.

Follow-up (07Mar2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from study site for protocol B1871047.
Updated information: lab data dated on 26Mar2021 updated, event verbatim updated from worsening of sub-mucosal gastric nodule to Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy of 26Mar2021).

Case Comment: Based on the available information, there was not reasonable possibility that the event "Worsening of sub-mucosal gastric nodule (GIST tumor type on biopsy)" as second primary malignancy was related to bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	26-MAR-2021	Biopsy GIST tumor type	Gastric nodule	
2	16-OCT-2020	Endoscopy upper gastrointestinal tract which increased of size.	a big sub-mucosal gastric nodule	
3	05-FEB-2021	Endoscopy upper gastrointestinal tract 5 cm of the fourth layer hypoechogenous evoking a gastrointestinal stromal tumor.	sub-mucosal tumour	

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	FRANCE		PRIVACY		Unk	Unk	Unk	25	JUN	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Pain in face [Facial pain]
Cramps [Muscle spasms]
Magnesium decreased [Blood magnesium decreased]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) TASIGNA (NILOTINIB HYDROCHLORIDE)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1)	#1) Unknown
#2)	#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown	#1) Unknown
#2) Unknown	#2) 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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200199678

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
28-JAN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200199678

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

B1871047.

A patient (no qualifiers provided) received bosutinib (BOSULIF); nilotinib hydrochloride (TASIGNA). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: MUSCLE SPASMS (non-serious) with onset 25Jun2019, outcome "unknown", described as "Cramps"; BLOOD MAGNESIUM DECREASED (non-serious) with onset 25Jun2019, outcome "unknown", described as "Magnesium decreased"; FACIAL PAIN (non-serious) with onset 25Jun2019, outcome "unknown", described as "Pain in face". The action taken for nilotinib hydrochloride was dosage reduced.

Additional information: The patient had discontinued bosutininb as required by protocol and was under nilotinib hydrochloride (TASIGNA) from an unspecified date. As of 24Sep2019 the patient experienced pain in face (TASIGNA discontinued then dose reduced), cramps and magnesium decreased.

The reporter's assessment of the causal relationship of "pain in face", "cramps" and "magnesium decreased" with the suspect product(s) bosutinib 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.

No follow-up attempts are needed. No further information is expected.

Case Comment: The information currently available is limited. Bosutinib administration dates, indication for use, medical history and concomitant medications were not reported. At this time there are no sufficient details supporting a causative role of bosutinib for the reported events.

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	FRANCE		PRIVACY		Unk	Female	Unk		JAN	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

a few episodes of bronchial superinfection [Bronchitis]
dysphonia [Dysphonia]
dyspnea [Dyspnoea]
infectious episode [Infection]
another infectious syndrome (bronchial or pseudo flu) [Infection]
depressive syndrome [Depression]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosutinib (BOSUTINIB) Unknown
#2) SPRYCEL (DASATINIB MONOHYDRATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) UNK
#2) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown
#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) Unknown / 25-OCT-2018
#2) Unknown

19. THERAPY DURATION
#1) 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
Unknown

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200199734

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-NOV-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

A female patient (unknown if pregnant) received bosutinib (BOSUTINIB), till 25Oct2018; dasatinib monohydrate (SPRYCEL), (Batch/Lot number: unknown). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: INFECTION (non-serious) with onset Jan2019, outcome "unknown", described as "another infectious syndrome (bronchial or pseudo flu)"; INFECTION (non-serious) with onset 2019, outcome "unknown", described as "infectious episode"; BRONCHITIS (non-serious) with onset Jan2020, outcome "unknown", described as "a few episodes of bronchial superinfection"; DYSPHONIA (non-serious), outcome "unknown"; DYSPNOEA (non-serious), outcome "not recovered", described as "dyspnea"; DEPRESSION (non-serious), outcome "unknown", described as "depressive syndrome". The action taken for dasatinib monohydrate was unknown.

The reporter's assessment of the causal relationship of "a few episodes of bronchial superinfection", "dysphonia", "dyspnea", "infectious episode", "another infectious syndrome (bronchial or pseudo flu)" and "depressive syndrome" with the suspect product(s) bosutinib 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: The patient was treated with SPRYCEL. At the specialist consultation on 02Jan2019, dysphonia and dyspnoea were reported. On 21Jan2019, dyspnea was still present, and an infectious episode was reported at the end of the year. Another infectious syndrome (bronchial or pseudo flu) was reported at the end of Jan2019. On 06Jan2020, a few episodes of bronchial superinfection and a depressive syndrome were reported. As of 26Sep2023, it was reported that the long term events are not reported by the center. The patient stopped Bosutinib and the last administration was on 25Oct2018. The long term events related to an infection were notified spontaneously during monitoring and will not be registered in the eCRF: Infectious syndrome in Jan2019 and bronchial superinfection in Jan2020. As of 14Nov2023, Comment for event a few episodes of bronchial superinfection: A history of current pneumonia before entering the study. A fungal infection after stopping bosutinib and not reported by the counter because long term follow-up. Reconcile with discrepancy. Site refuse to report AE after 28 days post bosutinib treatment. Comment for the events dyspnea; dysphonia; depressive syndrome; another infectious syndrome (bronchial or pseudo flu) and infectious episode: Reconcile with discrepancy. Site refuse to report AE after 28 days post bosutinib treatment.

Follow-up (26Sep2023): Updated information included a clarification received from the clinical team following a request regarding the event "Another infectious syndrome (bronchial or pseudo flu)".

Follow-up (14Nov2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information included: Event comment added.

Case Comment: All of the events are assessed as non serious and unrelated except for the event "a few episodes of bronchial superinfection" which is assessed as related. The unrelated events are most likely intercurrent medical conditions, unrelated to the suspect drug, bosutinib (BOSUTINIB). This case will be reassessed when further information is provided.

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	FRANCE		PRIVACY		69 Years	Female	57.00 kg	12	SEP	2019

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]
Osteoporosis [Osteoporosis]
pain on the right side of the lung [Pulmonary pain]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP)

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 07-MAR-2018 / 05-JUL-2018

19. THERAPY DURATION
#1) 3 months 29 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200207918

24c. DATE RECEIVED BY MANUFACTURER
01-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

for protocol B1871047.

A 69-year-old female patient received bosutinib (BOSULIF), from 07Mar2018 to 05Jul2018 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: CHEST PAIN (non-serious) with onset 12Sep2019, outcome "recovered" (2020); OSTEOPOROSIS (non-serious) with onset 18Sep2019, outcome "not recovered"; PULMONARY PAIN (non-serious) with onset Oct2020, outcome "recovered" (Oct2020), described as "pain on the right side of the lung".

The reporter considered "chest pain", "osteoporosis" and "pain on the right side of the lung" not related to bosutinib.

Additional information: The patient was no longer on bosutinib and without any treatment, some vague chest pains were reported on 12Sep2019, an osteoporosis problem on 18Sep2019 and pain on the right side of the lung end of Oct2020. All the events were rated non serious and grade 1. According to the investigator, these events were unrelated to the study drug bosutinib and unrelated to concomitant drug.

No follow-up attempts are needed. No further information is expected.

Case Comment: There is no temporal relationship between the events and administration of bosutinib. Bosutinib were discontinued for almost a year prior to the onset of the events in this report. The Company therefore considered that there was not a reasonable possibility that the events are associated with the study product or concomitant drugs.

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	FRANCE		PRIVACY		77 Years	Female	90.00 kg		JAN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Left hip pain [Arthralgia]
Anemia [Anaemia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 12-APR-2018 / 20-JUN-2018

19. THERAPY DURATION
#1) 2 months 9 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200208386

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200208386

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 77 year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 12Apr2018 (Batch/Lot number: unknown) to 20Jun2018 at 200 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ARTHRALGIA (hospitalization) with onset Jan2020, outcome "recovered" (04Aug2020), described as "Left hip pain"; ANAEMIA (non-serious) with onset 09Jun2020, outcome "recovered" (09Jun2020), described as "Anemia". Therapeutic measures were taken as a result of arthralgia, anaemia.

Additional information: events were rated as grade 3. For event "left hip pain", in Jan2020 hospitalization was required with hip prosthesis placement on 09Jun2020, no hip pain reported during the consultation of 04Aug2020. Report of hospitalization not available. For event "anemia", following of a hemorrhagic hip prosthesis, transfusional management of 3 erythrocyte concentrates in Jun2020.

The investigator considered the events were not related to study drug and concomitant drug.

No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the available information, the Company concurs with the investigator that there is not a reasonable possibility that the reported events Left hip pain, Anemia are related to the bosutinib. The events are more likely inter-current medical conditions.

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	FRANCE		PRIVACY		77 Years	Female	90.00 kg		OCT	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Left hip pain [Arthralgia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

A 77-year-old female patient (unknown if pregnant) received bosutinib

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 12-APR-2018 / 20-JUN-2018

19. THERAPY DURATION
#1) 2 months 9 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200208518

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(BOSULIF), from 12Apr2018 (Batch/Lot number: unknown) to 20Jun2018 at 200 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ARTHRALGIA (non-serious) with onset Oct2020, outcome "recovered" (Jan2021), described as "Left hip pain".

Additional information: Left hip pain, non-serious, grade 1. Loss of molecular response non-serious, grade 2. Events were unrelated to any concomitant drug

The investigator considered there was not a reasonable possibility that the events "left hip pain" and "loss of molecular response" were related to bosutinib.
No follow-up attempts are possible. No further information is expected.

Case Comment: Based on the information provided, the reported hip pain is likely an intercurrent medical condition in this 77 year old female patient and unrelated to bosutinib.

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	FRANCE		PRIVACY		77 Years	Female	90.00 kg		APR	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lower limbs edema [Oedema peripheral]
Generalized pruritus [Pruritus]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) GLIVEC (IMATINIB MESILATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 200 mg, 1x/day
#2)

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown
#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 12-APR-2018 / 20-JUN-2018
#2) Unknown

19. THERAPY DURATION
#1) 2 months 9 days
#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) ESIDREX (HYDROCHLOROTHIAZIDE) ; Unknown / APR-2019

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200208900

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
03-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 77-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 12Apr2018 to 20Jun2018 at 200 mg 1x/day; imatinib mesilate (GLIVEC). The patient's relevant medical history was not reported. Concomitant medication(s) included: ESIDREX, stop date: Apr2019.
The following information was reported: OEDEMA PERIPHERAL (non-serious) with onset Apr2019, outcome "recovered" (Sep2019), described as "Lower limbs edema"; PRURITUS (non-serious) with onset Sep2019, outcome "recovered" (Jan2020), described as "Generalized pruritus". The action taken for imatinib mesilate was dosage permanently withdrawn.

The reporter considered "lower limbs edema" and "generalized pruritus" not related to bosutinib.

Additional information: Lower limbs edema occurred following the withdrawal of diuretics (ESIDREX sopped in Apr2019), grade 2, non-serious, unrelated to the study drug bosulif or to a concomitant medication. Generalized pruritus, grade 2, non-serious, unrelated to the study drug, related to concomitant GLIVEC.

No follow-up attempts are needed. No further information is expected.

Case Comment: There is no temporal relationship between the events edema peripheral and pruritus and the administration of bosutinib. Bosutinib last dose was approximately 285 days prior to the onset of the events in this report. The Company therefore considered that there was not a reasonable possibility that the events edema peripheral and pruritus are associated with the study product, bosutinib.

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	FRANCE		PRIVACY		45 Years	Male	110.00 kg	12	JUN	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Weight loss [Weight decreased]
weight gain [Weight increased]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 12-DEC-2016 / 02-MAR-2017

19. THERAPY DURATION
#1) 2 months 19 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) SPRYCEL (DASATINIB MONOHYDRATE) ; 19-APR-2017 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200216040

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 45-year-old male patient received bosutinib (BOSULIF), from 12Dec2016 to 02Mar2017 at 200 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: SPRYCEL oral taken for chronic myeloid leukaemia, start date: 19Apr2017 (ongoing).
The following information was reported: WEIGHT INCREASED (non-serious) with onset 12Jun2017, outcome "recovered" (07May2018), described as "weight gain"; WEIGHT DECREASED (non-serious) with onset 2017, outcome "recovered" (02Mar2017), described as "Weight loss". The action taken for bosutinib was dosage not changed.

The reporter considered "weight loss" and "weight gain" not related to bosutinib.

Additional information: Weight loss was rated grade 2. Weight gain was rated grade 3. According to the investigator, the events were unrelated to study drug and to concomitant drug.
No follow-up attempts are needed. No further information is expected.

Case Comment: Based on the information provided, the reported events are likely intercurrent medical conditions and unrelated to the bosutinib.

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	FRANCE		PRIVACY		76 Years	Female	Unk		JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Lower limb oedema [Oedema peripheral]
Eyelid edema [Eyelid oedema]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 200 mg, 1x/day	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 03-MAY-2019 / 01-AUG-2019	#1) 2 months 30 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	Relevant Med History	none ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200216414

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200216414

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 76-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), first regimen from 03May2019 to 01Aug2019 at 200 mg 1x/day, second regimen from 02Aug2019 to 22Oct2020 at 300 mg 1x/day and third regimen since 23Oct2020 (ongoing) at 200 mg 1x/day. The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: OEDEMA PERIPHERAL (non-serious) with onset Jun2020, outcome "recovered" (Aug2021), described as "Lower limb oedema"; EYELID OEDEMA (non-serious) with onset 29Jun2021, outcome "recovered" (Aug2021), described as "Eyelid edema". The action taken for bosutinib was dosage not changed.

The reporter considered "lower limb oedema" not related to bosutinib. The reporter considered "eyelid edema" related to bosutinib.
Additional information: the events lower limb oedema and eyelid edema were rated grade 1.

No follow-up attempts are needed. No further information is expected.

Case Comment: Based on the information provided and known safety profile, there is a reasonable possibility that the reported events are related to bosutinib.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, 1x/day; Unknown	Unknown	02-AUG-2019 / 22-OCT-2020; 1 year 2 months 21 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, 1x/day; Unknown	Unknown	23-OCT-2020 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		45 Years	Male	110.00 kg	17	MAR	2017

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Renal failure degradation grade 2 [Renal failure]
Dermatitis grade 1 [Dermatitis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 12-DEC-2016 / 02-MAR-2017

19. THERAPY DURATION
#1) 2 months 19 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) SPRYCEL (DASATINIB MONOHYDRATE) ; 19-APR-2017 / 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200216666

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
04-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 45 year-old male patient received bosutinib (BOSULIF), from 12Dec2016 (Batch/Lot number: unknown) to 02Mar2017 at 200 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: SPRYCEL taken for chronic myeloid leukaemia, start date: 19Apr2017 (ongoing).
The following information was reported: RENAL FAILURE (non-serious) with onset 17Mar2017, outcome "not recovered", described as "Renal failure degradation grade 2"; DERMATITIS (non-serious) with onset Nov2017, outcome "recovered" (Jan2018), described as "Dermatitis grade 1".

The investigator considered there was not a reasonable possibility that the events "renal failure degradation grade 2" and "dermatitis grade 1" were related to bosutinib nor concomitant medication.

No follow-up attempts are possible. No further information is expected.

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	FRANCE		PRIVACY		65 Years	Female	50.00 kg		OCT	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Voice disorder [Dysphonia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report received from a contactable reporter(s) (Physician) for protocol B1871047.

A 65-year-old female patient received bosutinib (BOSULIF), from

(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) Bosulif (BOSUTINIB) Film-coated tablet

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 300 mg, daily

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) 13-FEB-2019 / 02-MAR-2019

19. THERAPY DURATION
#1) 18 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
APR-2020 to APR-2020	Relevant Med History	Thyroid nodule removal (Thyroid nodule removal)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200225534

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
07-MAR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

13Feb2019 to 02Mar2019 at 300 mg daily. The patient's relevant medical history included: "thyroid nodule surgery", start date: Apr2020, stop date: Apr2020. The patient's concomitant medications were not reported.
The following information was reported: DYSPHONIA (non-serious) with onset Oct2020, outcome "recovered" (Dec2020), described as "Voice disorder".
Additional information: The patient was on long-term follow-up and on TASIGNA. Operated thyroid nodule in Apr2020, having caused voice disorders in Oct2020. The event voice disorder was rated as grade 1, assessed as non-serious.

The reporter considered "voice disorder" not related to bosutinib.

Follow-up attempts are completed. No further information is expected.

Follow-up (30May2022): This is a follow-up to a non-interventional study report for protocol B1871047:
Updated information: Reaction data (new event Epigastric pain added), relevant medical history (Intermittent epigastric pain removed).

Follow-up (07Mar2023). This is a non-interventional study report received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information included: Bosutinib start date updated to 13Feb2019 and event 'Epigastric pain' deleted.

Case Comment: Based on the information currently available and in concurrence with reporting investigator, the reported 'voice disorder' is deemed unrelated to study drug bosutinib. Event is likely due to an intercurrent condition; the mentioned surgery on thyroid nodule may provide alternative explanation.

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	FRANCE		PRIVACY		34 Years	Male	115.00 kg	23	DEC	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

COVID-19 [COVID-19]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 09-SEP-2019 / 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
23-DEC-2021 to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)
Unknown	Past Drug Event 2 injections received	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200261248

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
10-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200261248

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 34-year-old male patient received bosutinib (BOSULIF), since 09Sep2019 (ongoing) at 500 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia", start date: 23Dec2021 (ongoing). The patient's concomitant medications were not reported. Past drug history included: Covid-19 vaccine for COVID-19 immunization, notes: 2 injections received.
The following information was reported: COVID-19 (non-serious) with onset 23Dec2021, outcome "recovered" (27Dec2021). The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of covid-19.

The reporter considered "covid-19" not related to bosutinib.
Additional information: COVID-19 contracted despite vaccination up to date (2 injection of vaccine). COVID-19 grade 2. Oral DOLIPRANE was received from 23Dec2021 to 27Dec2021 for fever. According to the investigator, the event was not related to study drug or concomitant medication.

No follow-up attempts are needed. No further information is expected.

Case Comment: In concurrence with the reporting investigator, the Company considers the reported COVID-19 is unrelated to suspect drug bosutinib administration. The patient contracted COVID-19 amid coronavirus pandemic.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event 2 injections received	COVID-19 vaccine (COVID-19 VACCINE); Drug Indication: COVID-19 immunization (COVID-19 immunisation)

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	FRANCE		PRIVACY		64 Years	Female	50.00 kg	16	SEP	2019

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Asthenia [Asthenia]
Asthenia [Asthenia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 13-FEB-2019 / 02-MAR-2019

19. THERAPY DURATION
#1) 18 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200271630

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200271630

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 64-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), from 13Feb2019 to 02Mar2019 at 300 mg daily.
The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ASTHENIA (non-serious) with onset 16Sep2019, outcome "recovered" (Oct2019), ASTHENIA (non-serious) with onset 22Apr2020, outcome "recovered" (Jun2020) and all described as "Asthenia".

The reporter considered "asthenia" not related to bosutinib.

Additional information: Both episodes of asthenia were grade 1. Causality assessment was unrelated to study drug and concomitant treatments for both episodes of asthenia.

No follow-up attempts are needed. No further information is expected.

Follow-up (07Mar2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information included: start date of bosutinib updated.

Follow-up (09Mar2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: onset date of first episode of asthenia (updated from "16Mar2019" to "16Sep2019").

Case Comment: Based on temporal association, the episodes of asthenia are deemed unrelated to bosutinib as the events occurred 6 months 15 days and 1 year 1 month 21 days from the last dose of bosutinib.

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	FRANCE		PRIVACY		73 Years	Female	86.00 kg			2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

MYCOSIS OF THE INGUINAL FOLDS [Fungal infection]
PAROXYSTIC ATRIAL FIBRILLATION [Atrial fibrillation]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 09-DEC-2019 / DEC-2020

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) BISOPROLOL (BISOPROLOL) ; MAR-2020 / Ongoing
#2) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; DEC-1999 / Ongoing
#3) FLECAINE (FLECAINIDE ACETATE) ; MAR-2014 / Ongoing
#4) IMODIUM (LOPERAMIDE HYDROCHLORIDE) ; JAN-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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200277635

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
14-FEB-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73 year-old female patient received bosutinib (BOSULIF), from 09Dec2019 (Batch/Lot number: unknown) to Dec2020 at 200 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: BISOPROLOL taken for hypertension, start date: Mar2020 (ongoing); LEVOTHYROX taken for hypothyroidism, start date: Dec1999 (ongoing); FLECAINE taken for heart rate abnormal, start date: Mar2014 (ongoing); IMODIUM taken for diarrhoea, start date: Jan2016 (ongoing).
The following information was reported: FUNGAL INFECTION (non-serious) with onset Jan2021, outcome "recovered" (2021), described as "MYCOSIS OF THE INGUINAL FOLDS"; ATRIAL FIBRILLATION (non-serious) with onset 2020, outcome "recovered" (Jan2021), described as "PAROXYSTIC ATRIAL FIBRILLATION".

Additional information: The event "mycosis of the inguinal folds" was rated non-serious with grade 1 and the event "paroxystic atrial fibrillation" was rated non-serious with grade 2.

According to the investigator, both events were unrelated to the study drug bosutinib and unrelated to concomitant drugs.

No follow-up attempts are possible. No further information is expected.

Case Comment: There is insufficient information to attribute the causality of events, Atrial fibrillation and Fungal infection, to the suspect drug Bosutinib malate. Medical history was not provided, however, the Subject is on concomitant medications for hypertension, hypothyroidism and abnormal heart rate, suggestive of medical conditions which may provide a plausible alternative cause for 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
PRIVACY	FRANCE		PRIVACY		74 Years	Female	86.00 kg	14	JUN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

POLYPS [Polyp]
INCREASE OF ATHEROMA PLAQUES [Arteriosclerosis]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 09-DEC-2019 / DEC-2020

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) NILOTINIB (NILOTINIB) ; Ongoing
#2) ELIQUIS (APIXABAN) ; Ongoing
#3) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; Ongoing
#4) ASPIRINE (ACETYLSALICYLIC ACID) ; 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200277734

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200277734

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 74 year-old female patient received bosutinib (BOSULIF), from 09Dec2019 (Batch/Lot number: unknown) to Dec2020 at 200 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: NILOTINIB (ongoing); ELIQUIS (ongoing); LEVOTHYROX (ongoing); ASPIRINE (ongoing).
The following information was reported: POLYP (hospitalization) with onset 11Sep2021, outcome "recovered" (06Jan2022), described as "POLYPS"; ARTERIOSCLEROSIS (medically significant) with onset 14Jun2021, outcome "not recovered", described as "INCREASE OF ATHEROMA PLAQUES". The patient underwent the following laboratory tests and procedures: colonoscopy: (11Sep2021) discovery of two polyps. The action taken in response to these events for the study drug bosutinib was not applicable. Additional information: it was reported "discovery during a colonoscopy on 11Sep2021 of two polyps, the first of which was removed on the same day and the second polyp was removed during the hospitalization of 06Jan2022". The event polyps was rated serious (hospitalization) with grade 3 and the event "increase of atheroma plaques" was rated non-serious with grade 4. In follow-up information received on 04Apr2022, it was reported there is no severity criterion noted in the hospital file and in the CRF (Case Report Form). The increase in atheroma plaques was seen only on the ultrasound of 14Jun2021. According to the investigator, both events were unrelated to the study drug bosutinib and unrelated to concomitant drugs. In follow-up dated 07Sep2022, was reported that increase of atheroma plaques was rated grade 2.
No follow-up attempts are possible. No further information is expected.

Follow-up (04Apr2022): New information was received in response to a query reporting information regarding event severity and that atheroma plaques was seen only on the ultrasound of 14Jun2021.

Follow-up (07Sep2022): This is a follow-up non-interventional study report (Post Authorization Safety Study) received from the CRO for protocol B1871047. Updated information: grade of one event.

Case Comment: The company deemed that there is not a reasonable possibility that the events POLYPS and INCREASE OF ATHEROMA PLAQUES were related to Pfizer study drug BOSUTINIB. The event mostly represented an intercurrent condition in this patient.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	11-SEP-2021	Colonoscopy	Discovery of two polyps	
2	14-JUN-2021	Ultrasound scan	Increase in atheroma plaques	

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	FRANCE		PRIVACY		71 Years	Male	114.00 kg		NOV	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

DYSPNEA ON EFFORT [Dyspnoea exertional]
Lower limb pain [Pain in extremity]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 300 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 12-NOV-2020 / 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	Past Drug Event Dyspnea on 05Nov2020	

(Continued on Additional Information Page)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200282097

24c. DATE RECEIVED BY MANUFACTURER
26-OCT-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 71-year-old male patient received bosutinib (BOSULIF), since 12Nov2020 (ongoing) at 300 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported. Past drug history included: Dasatinib, reaction(s): "Dyspnea", notes: Dyspnea on 05Nov2020.
The following information was reported: DYSPNOEA EXERTIONAL (non-serious) with onset Nov2021, outcome "not recovered", described as "DYSPNEA ON EFFORT"; PAIN IN EXTREMITY (non-serious) with onset Nov2021, outcome "not recovered", described as "Lower limb pain". The action taken for bosutinib was dosage not changed.

The reporter considered "dyspnea on effort" and "lower limb pain" not related to bosutinib.

Additional information: The events dyspnoea on effort and lower limb pain were rated grade 1. Action taken with bosutinib in response to both events was dose not changed. Events reported as non-serious. The investigator considered that the event was unrelated to any concomitant drug.

Follow-up (15Sep2022): This is a non-interventional study report (Post Authorization Safety Study) received from CRO for protocol B1871047.
Updated information: primary reporter details updated, new reporter added, patient details (DOB, weight and height) added, dosage of bosutinib added, event verbatim changed from dyspnoea to dyspnoea on effort, start date of events dyspnoea on effort and lower limb pain updated to Nov2020 and outcome updated as not recovered (previously unknown), and causality for both events updated as unrelated (previously not reported).

Amendment: This follow-up report is being submitted to amend previous information: onset date for both events corrected to Nov2021.

Case Comment: Based on the available information, the Company considers the reported events "dyspnea on effort" and "lower limb pain" are unrelated to suspect drug bosutinib but more likely due to underlying or inter-current medical conditions.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Past Drug Event Dyspnea on 05Nov2020	DASATINIB (DASATINIB); Drug Reaction: Dyspnea (Dyspnoea)

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	FRANCE		PRIVACY		77 Years	Male	78.80 kg		JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Digestive disorder [Gastrointestinal disorder]
Diastasis [Diastasis recti abdominis]
Back pain, low dorsalgia on discopathy MODIC 1 (T6-T7-T8) [Back pain]
Scalp infection [Skin infection]
Dyspnea [Dyspnoea]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200282099

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047.

A 77-year-old male patient received bosutinib (BOSULIF). The patient's relevant medical history and concomitant medications were not reported.

The following information was reported: BACK PAIN (non-serious) with onset Jun2020, outcome "recovering"; described as "Back pain, low dorsalgia on discopathy MODIC 1 (T6-T7-T8) "; DIASTASIS RECTI ABDOMINIS (non-serious) with onset Dec2020, outcome "unknown", described as "Diastasis"; GASTROINTESTINAL DISORDER (non-serious) with onset Dec2020, outcome "recovered" (May2021), described as "Digestive disorder"; SKIN INFECTION (non-serious) with onset 06Nov2021, outcome "recovered" (18Nov2021), described as "Scalp infection"; DYSPNOEA (non-serious) with onset 21Mar2022, outcome "recovering", described as "Dyspnea". The action taken for bosutinib was dosage not changed.

Additional information: The patient was on bosutinib. It was noted digestive disorders from Dec2020 to May2021, in Dec2020 back pain for 6 months and diastasis. Scalp infection was grade 1 from 06Nov2021 to 18Nov2021. Event dyspnea on 21Mar2022 was grade 1.

The reporter considered "digestive disorder" related to bosutinib. The reporter considered "back pain, low dorsalgia on discopathy modic 1 (t6-t7-t8) ", "scalp infection" and "dyspnea" not related to bosutinib or to concomitant treatment.
The reporter's assessment of the causal relationship of "diastasis" with the suspect product(s) bosutinib 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 (02Jun2022). This follow-up is received from the investigational site via CRO. Updated information included: patient's details, details on 'scalp infection', new event (dyspnea). Causality for some events.

Follow-up (07Sep2022). This is a follow-up received from the CRO.
This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047.

Updated information includes: patient weight updated; updated start date for the event low back pain (from 2020 to Jun2020) and updated outcome (from unknown to recovering), investigator causality assessment for digestive disorder and lower back pain, updated description of the event back pain.

Case Comment: Based on available information, a possible contributory role of the subject drug BOSUTINIB cannot be excluded for the reported events Digestive disorder and diastasis. The events back pain, scalp infection and dyspnea were not related to bosutinib. This case will be re-assessed should additional information become available.

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	FRANCE		PRIVACY		76 Years	Female	52.00 kg	04	MAR	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

diarrhea [Diarrhoea]
Cephalgia [Headache]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG?
☒ YES ☐ NO ☐ NA

15. DAILY DOSE(S)
#1) 200 mg, daily

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) 17-DEC-2020 / 07-APR-2021

19. THERAPY DURATION
#1) 3 months 22 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200282100

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-NOV-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 76-year-old female patient received bosutinib (BOSULIF), first regimen from 17Dec2020 to 07Apr2021 at 200 mg daily and second regimen from 08Apr2021 to 30Jun2022 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: HEADACHE (non-serious) with onset 04Mar2021, outcome "recovered" (Apr2021), described as "Cephalgia"; DIARRHOEA (non-serious) with onset Sep2021, outcome "recovered" (Jul2022), described as "diarrhea". The action taken for bosutinib was dosage permanently withdrawn on 30Jun2022.

The reporter considered "diarrhea" related to bosutinib. The reporter considered "cephalgia" not related to bosutinib.

Additional information: Bosutinib has not been reintroduced.

Follow-up attempts are completed. No further information is expected.

Follow-up (05Jul2022): New information received from the CRO.
Updated information included: The event cephalgia resolved in Apr2021.

Follow-up (06Sep2022): This is a follow-up Non-Interventional Study report (Post Authorization Safety Study) for protocol B1871047.
Updated information received from the CRO includes event outcome for diarrhea and headache and action taken for bosutinib.

Follow-up (10May2023): This is a follow-up Non-Interventional Study report (Post Authorization Safety Study) for protocol B1871047.
Updated information received from the CRO included: The event headache resolved in Apr2021.

Follow-up attempts are completed. No further information is expected.

Amendment: This follow-up report is being submitted to amend previously reported information: date of Birth was corrected (the patient's age was therefore 76 years old).

Follow-up (18Jul2023): This is a follow-up Non-Interventional Study report received from investigational site via CRO included:
Update information: Bosulif from 08Apr2021 at 300mg daily.

Follow-up (07Sep2023, 07Sep2023): This is a follow-up Non-Interventional Study report received from investigational site via CRO and a follow-up Non-Interventional Study report received from clinical team :
Update information: new reporter (slide 2), dosage regimen for Bosulif (new first regimen). stop date for second regimen for Bosulif.

Follow-up (30Nov2023) : This is a follow-up Non-Interventional Study report received from investigational site via CRO.
Updated information: clinical course.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the information currently available and known product safety profile, a causal association between the study drug bosutinib and the reported events 'diarrhea' and 'cephalgia' cannot be completely excluded.
The follow-up information received does not alter the previous company clinical evaluation.

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	300 mg, daily; Unknown	Unknown	08-APR-2021 / 30-JUN-2022; 1 year 2 months 23 days

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	FRANCE		PRIVACY		77 Years	Female	52.10 kg		SEP	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Numerous functional complaints (limb pain) [Pain in extremity]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200282102

24c. DATE RECEIVED BY MANUFACTURER
02-JUN-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 77-year-old female patient (unknown if pregnant) received bosutinib (BOSUTINIB). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: PAIN IN EXTREMITY (non-serious) with onset Sep2021, outcome "unknown", described as "Numerous functional complaints (limb pain)".

The reporter considered "numerous functional complaints (limb pain)" not related to bosutinib.
Follow-up attempts are completed. No further information is expected.

Additional information: The event was assessed as non-serious and rated as grade 2. According to the reporter, the event was not related to study drug or concomitant medication.

No follow-up attempts are needed. No further information is expected.

Amendment: This follow-up report is being submitted to amend previously reported information: patient's year of birth updated and accordingly patient's age updated from 27-year-old to 77-year-old, and patient's height updated.

Case Comment: Event numerous functional complaints (limb pain) represents an intercurrent medical condition and unrelated to bosutinib .

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	FRANCE		PRIVACY		73 Years	Female	86.00 kg		DEC	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

HYPOTENSION [Hypotension]
FATIGUE [Fatigue]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Unknown
#2) PERINDOPRIL (PERINDOPRIL)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 200 mg, daily
#2) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown
#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 09-DEC-2019 / DEC-2020
#2) Unknown

19. THERAPY DURATION
#1) Unknown
#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) NILOTINIB (NILOTINIB) ; Unknown
#2) FLECAINE (FLECAINIDE ACETATE) ; Unknown
#3) LEVOTHYROX (LEVOTHYROXINE SODIUM) ; Unknown
#4) BISOPROLOL (BISOPROLOL) ; 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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200285906

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
17-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old female patient received bosutinib (BOSUTINIB), from 09Dec2019 to Dec2020 at 200 mg daily; perindopril (PERINDOPRIL), (Batch/Lot number: unknown). The patient's relevant medical history was not reported. Concomitant medication(s) included: NILOTINIB; FLECAINE; LEVOTHYROX; BISOPROLOL.
The following information was reported: HYPOTENSION (non-serious) with onset Dec2020, outcome "recovered" (Dec2020); FATIGUE (non-serious) with onset 16Apr2021, outcome "recovered" (2021). The action taken for perindopril was dosage reduced.

The reporter considered "hypotension" and "fatigue" not related to bosutinib.

Additional information: Hypotension, grade 1, unrelated to the study drug bosutinib, related to concomitant perindopril. Fatigue, grade1, unrelated to the study drug bosutinib or concomitant medications.

Follow-up (07Sep2022): This is a follow-up report received from the CRO.
Updated information includes: for event fatigue updated outcome to not recovered (stop date delated)

Follow-up (17Jul2023): This is a follow-up to a non-interventional study for protocol B1871047 received from investigator site via the CRO. Updated information: outcome of event fatigue.

No follow-up attempt is needed. No further information is expected.

Case Comment: There is insufficient evidence to demonstrate that the adverse events hypotension and fatigue were related to bosutinib. Based on the available information and in agreement with the reporter this case is considered as not related to suspect drug. 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			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
PRIVACY	FRANCE		PRIVACY		74 Years	Female	86.00 kg	10	JAN	2022

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Skin xerosis on the trunk and face [Dry skin]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1) 200 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 09-DEC-2019 / DEC-2020

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) PERINDOPRIL (PERINDOPRIL) ; Ongoing
#2) NILOTINIB (NILOTINIB) ; Ongoing
#3) FLECAINE (FLECAINIDE ACETATE) ; Ongoing
#4) ELIQUIS (APIXABAN) ; 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

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200286823

24c. DATE RECEIVED BY MANUFACTURER
07-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 74-year-old female patient (unknown if pregnant) received bosutinib (BOSUTINIB), from 09Dec2019 to Dec2020 at 200 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: PERINDOPRIL (ongoing); NILOTINIB (ongoing); FLECAINE (ongoing); ELIQUIS (ongoing). The following information was reported: DRY SKIN (non-serious) with onset 10Jan2022, outcome "recovered" (12Apr2022), described as "Skin xerosis on the trunk and face".

The reporter considered "skin xerosis on the trunk and face" not related to bosutinib.

Additional information: Skin xerosis on the trunk and face, grade 1, non-serious, unrelated to the study drug or concomitant medications. The event dry skin was rated grade 1. The event dry skin outcome was not recovered. Action taken not applicable. Event dry skin was reported as non-serious. The investigator considered that the event dry skin was unrelated to Bostunib or to any concomitnant drug. Event description was provided as AE6A CUTANEOUS XEROSIS ACCOMPANIED BY ECZEMATIFORM LESIONS AND SCRATCHING LESIONS. Dry skin was reported as non clinically significative in the medical file.

No follow-up attempts are needed. No further information is expected.

Follow-up (07Sep2022): This is a non-interventional study follow-up report received from the CRO.
Updated information includes: Outcome for event CUTANEOUS XEROSIS ON TRUNK AND FACE updated to recovered on 12Apr2022; new event added: dry skin (start on 28Jan2022, outcome not recovered, non serious).

Follow-up (07Sep2023): This is a non-interventional study follow-up report received from the clinical team.
Updated information included: event dry skin (start on 28Jan2022) deleted.

Case Comment: Based on the available information, the Company considers the reported event 'skin xerosis on the trunk and face' is unrelated to suspect drug bosutinib but more likely an inter-current medical condition.

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	FRANCE		PRIVACY		48 Years	Female	59.50 kg	17	FEB	2022

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

hepatic cytolysis [Hepatic cytolysis]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(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) 500 mg, daily	#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☒ NO ☐ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) MAR-2020 / 18-FEB-2022	#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
15-MAR-2021 to Ongoing	Relevant Med History	Colitis (Colitis)
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200345760

24c. DATE RECEIVED BY MANUFACTURER
28-SEP-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 48-year-old female patient received bosutinib (BOSULIF), first regimen from Mar2020 to 18Feb2022 at 500 mg daily and second regimen since 28Feb2022 at 400 mg 1x/day. The patient's relevant medical history included: "EDEMATO CONGESTIVE COLITIS", start date: 15Mar2021 (ongoing); "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported. The following information was reported: HEPATIC CYTOLYSIS (non-serious) with onset 17Feb2022, outcome "recovered" (28Feb2022). Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage reduced.

The reporter considered "hepatic cytolysis" related to bosutinib.

Reporter Comment: withdrawal of bosutinib from 18Feb2022 to 28Feb2022; resumption at 400 mg daily after phone advice from the patient's hematologist. Consultation by phone since the increased of AST and ALT. Waiting for additional information for possible other cause.

Additional information: Readministration of bosutinib on 28Feb2022 following ALAT/ASAT stabilization. Event Hepatic cytolysis was rated grade 3. Biology of 21Feb2022 (grade 3). Rechallenge was negative.

Follow-up(17May2022): New information received from investiational site via CRO. Updated information: hepatic cytolysis outcome updated to recovered on 28Feb2022, and clinical course provided.

Follow-up (12Jul2023): This is a follow-up to a non-interventional study for protocol B1871047 received from investigational site via CRO. Updated information includes: Lab data (additional AST and ALT values, previously reported values of AST and ALT were corrected).

No follow-up attempt is needed. No further information expected.

Follow-up (26Jul2023): new information received from the investigator via the CRO. Updated information included patient's weight, clinical details.

Follow-up attempts are completed. No further information is expected.

Follow-up (28Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: medical history added (Chronic myeloid leukemia).

Follow-up (28Sep2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information includes start date and daily dose of the first bosutinib dosage regimen and action taken updated from "Temporarily withdrawn" to "Dose reduced".

Case Comment: Based on a plausible temporal relationship, causality for the onset of grade 2 hepatic cytolysis secondary to Bosutinib cannot be ruled out. The underlying malignancy may be contributory. 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-FEB-2022	Alanine aminotransferase	275	
2	21-FEB-2022	Alanine aminotransferase	318	
3	28-FEB-2022	Alanine aminotransferase	123	
4	17-FEB-2022	Aspartate aminotransferase	131	
5	21-FEB-2022	Aspartate aminotransferase	114	
6	28-FEB-2022	Aspartate aminotransferase	48	
7	18-FEB-2022	Ultrasound abdomen	non-complicated chelestiasis	

Mfr. Control Number: 202200345760

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) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	400 mg, 1x/day; Unknown	Unknown	28-FEB-2022 / Unknown; 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
PRIVACY	FRANCE		PRIVACY		76 Years	Male	97.00 kg		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

CHRONIC ANTRAL GASTRITIS [Chronic gastritis]
Rectal polyp [Rectal polyp]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

The initial case was missing the following minimum criteria: adverse event unspecified. Upon receipt of follow-up information on 01Mar2022, this case now contains all required information to be considered valid.

(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) Bosulif (BOSUTINIB) Film-coated tablet

(Continued on Additional Information Page)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)
#1) 200 mg, daily

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) 24-MAR-2021 / 27-FEB-2022

19. THERAPY DURATION
#1) 11 months 4 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) XARELTO (RIVAROXABAN) ; 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 recovered	Bladder carcinoma (Bladder cancer)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200347155

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
21-JUL-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200347155

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

A 76-year-old male patient received bosutinib (BOSULIF), first regimen from 24Mar2021 to 27Feb2022 at 200 mg daily, second regimen since 28Feb2022 (ongoing) at 200 mg (200 mg, monday, tuesday, wednesday, thursday and friday) and third regimen since 28Feb2022 (ongoing) at 300 mg (300 mg, saturday and sunday). The patient's relevant medical history included: "BLADDER CARCINOMA" (not ongoing), notes: recovered. Concomitant medication(s) included: XARELTO taken for iron deficiency anaemia. The following information was reported: CHRONIC GASTRITIS (non-serious), outcome "recovered", described as "CHRONIC ANTRAL GASTRITIS"; RECTAL POLYP (non-serious), outcome "recovered" (18Feb2022). Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of rectal polyp.
Additional information: event chronic antral gastritis was assessed as non-serious and grade 1, rectal polyp was non-serious and grade 2. Coloscopy performed on 18Feb2022 was within the limits of normal with removal of a rectal polyp. The coloscopy scheduled for 18Feb2022 (anemia Microcytic ferridefy, under xarelto): Fibroscopie Oeso-Gastro-Duodenale (FOGD): Normal, colonoscopy: ablation of a small polyp. Clinical examination: weight 91 kg, ps (performance status 0). In the conclusion of the hystological examination of 18Feb2022: chronic antral gastritis of moderate intensity of mild activity, without intestinal atrophy or metaplasia, asymptomatic patient.

The reporter considered "chronic antral gastritis" and "rectal polyp" not related to bosutinib.
No follow-up attempts are possible. No further information is expected.

Follow-up (12Jul2023): This is a follow-up report received from the CRO.
Updated information included: suspect drug Bosulif details (Action Taken: Dose Not Changed).

Follow-up (21Jul2023): This is a follow-up report received from the investigator. Updated information included: updated dosage regimens, updated description of lab tests, additional lab data.

Case Comment: Based on the available information and action taken, there was no reasonable possibility that the events "chronic antral gastritis" and "rectal polyp" were related to bosutinib or concomitant drugs. This case will be re-assessed should additional information become available. 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	18-FEB-2022	Colonoscopy within the limits of normal. removal of a rectal polyp	normal	
2		Eastern Cooperative Oncology Group performance status	0	
3	18-FEB-2022	Histology	chronic antral gastritis of moderate intensity of chronic antral gastritis of moderate intensity of mild activity, without atrophy nor intestinal metaplasia asymptomatic patient	
4		Oesophagogastroduodenoscopy	normal	
5		Weight	91 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) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, Monday,	Unknown	28-FEB-2022 /

Mfr. Control Number: 202200347155

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
Regimen #2	Tuesday, Wednesday, Thursday and Friday; Unknown		Ongoing; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, Saturday and Sunday; Unknown	Unknown	28-FEB-2022 / Ongoing; 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
PRIVACY	FRANCE		PRIVACY		72 Years	Male	Unk	22	MAY	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Dyspnea [Dyspnoea]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1)

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

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
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200372745

24c. DATE RECEIVED BY MANUFACTURER
04-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200372745

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 72-year-old male patient received bosutinib (BOSULIF). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DYSPNOEA (non-serious) with onset 22May2021, outcome "recovered" (21Jul2021), described as "Dyspnea". The action taken for bosutinib was dosage not changed.
According to the investigator event was related to study drug and unrelated to concomitant treatment.

Additional information: the event dyspnea was grade 2.

No follow-up attempts are needed. No further information is expected.

Case Comment: Based on available information and known AE profile of bosutinib, the reasonable possibility of an association between Dyspnea and suspect product cannot be ruled out.

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	FRANCE		PRIVACY		74 Years	Male	Unk	14	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

MINIMAL SKIN LESIONS [Skin lesion]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) GLIVEC (IMATINIB MESILATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2) UNK	#2) Unknown

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) 07-NOV-2019 / 03-DEC-2019	#1) 27 days
#2) 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
2011 to 2011	Relevant Med History operated	Abdominal aortic aneurysm (Aortic aneurysm)
2019 to 2019	Relevant Med History ENDARTERECTOMY	Carotid artery occlusion (Carotid artery occlusion)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391789

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200391789

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 74-year-old male patient received bosutinib (BOSULIF), from 07Nov2019 to 03Dec2019 at 500 mg 1x/day; imatinib mesilate (GLIVEC), (Batch/Lot number: unknown). The patient's relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011, notes: operated; "LEFT INTERNAL CAROTID ARTERY BLOCKED", start date: 2019, stop date: 2019, notes: ENDARTERECTOMY; "ENDARTERECTOMY" (unspecified if ongoing). The patient's concomitant medications were not reported.
The following information was reported: SKIN LESION (non-serious) with onset 14Jan2021, outcome "recovered" (08Apr2021), described as "MINIMAL SKIN LESIONS". The action taken for imatinib mesilate was dosage not changed.
Additional information: minimal skin lesions were non-serious, grade 1, unrelated to bosutinb and related to concomitant drug GLIVEC. The site described: during the consultation of 14Jan2021, the patient presented some minimal skin lesions on the arms and legs that were not pruritic without argument for a toxidermia. No additional concomitant treatments or modification of current treatments.

The reporter considered "minimal skin lesions" not related to bosutinib.

No follow-up attempts are possible. No further information is expected.

Case Comment: In concurrence with the reporter, the reported event 'minimal skin lesions' is unrelated to the administration of bosutinib. The event occurred more than 1 year after the last dose of bosutinib. The patient's other medication may provide an explanation for the event.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		75 Years	Male	Unk	21	OCT	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

purpura [Purpura]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) GLIVEC (IMATINIB MESILATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2) UNK	#2) Unknown

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) 07-NOV-2019 / 03-DEC-2019	#1) 27 days
#2) 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
2011 to 2011	Relevant Med History operated	Abdominal aortic aneurysm (Aortic aneurysm)
2019 to 2019	Relevant Med History ENDARTERECTOMY	Carotid artery occlusion (Carotid artery occlusion)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391824

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200391824

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), from 07Nov2019 to 03Dec2019 at 500 mg 1x/day; imatinib mesilate (GLIVEC), (Batch/Lot number: unknown). The patient's relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011, notes: operated; "LEFT INTERNAL CAROTID ARTERY BLOCKED", start date: 2019, stop date: 2019, notes: ENDARTERECTOMY; "ENDARTERECTOMY" (unspecified if ongoing). The patient's concomitant medications were not reported.
The following information was reported: PURPURA (non-serious) with onset 21Oct2021, outcome "recovered" (27Jan2022). The action taken for bosutinib was unknown; for imatinib mesilate was dosage not changed.

The reporter considered "purpura" not related to bosutinib.

Additional information: event was non-serious, rated grade 1, unrelated to bosutinib and related to concomitant drug GLIVEC.
The site described: the patient presented during the consultation of 21Oct2021 a purpura of the upper limbs.

Case Comment: Based on the available information, the event purpura is not related to bosutinib. The last dose of bosutinib was administered on 03DEC2019.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		75 Years	Male	Unk	06	SEP	2021

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
HYPOACOUSIA [Hypoacusis]

Case Description: The initial safety information received was reporting only non-serious adverse drug reaction(s), Upon receipt of follow-up information on [14Mar2022], this case now contains serious adverse reaction(s). Information processed together.

OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 07-NOV-2019 / 03-DEC-2019

19. THERAPY DURATION
#1) 27 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
2011 to 2011	Relevant Med History	Abdominal aortic aneurysm (Aortic aneurysm)
Unknown	Relevant Med History	Aneurysmectomy (Aneurysmectomy)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391860

24c. DATE RECEIVED BY MANUFACTURER
14-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200391860

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

A 75 year-old male patient received bosutinib (BOSULIF), from 07Nov2019 (Batch/Lot number: unknown) to 03Dec2019 at 500 mg 1x/day. Relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011; "OPERATED ABDOMINAL AORTIC ANEURYSM" (unspecified if ongoing); "LEFT INTERNAL CAROTID BLOCKED", start date: 2019, stop date: 2019; "Endarterectomy" (unspecified if ongoing). There were no concomitant medications.
The following information was reported: HYPOACUSIS (medically significant) with onset 06Sep2021, outcome "recovered" (16Sep2021), described as "HYPOACOUSIA". Therapeutic measures were taken as a result of hypoacusis. The patient went to the emergency on 13Sep2021 for hypoacousia for a week. Cerumen plug in the left ear: physiological serum 5 times a day then extraction of the plug by the doctor in 48 or 72 hours.

The investigator considered there was not a reasonable possibility that the event "hypoacousia" was related to bosutinib.
No follow-up attempts are possible. No further information is expected.

Case Comment: In concurrence with the investigator, the reported 'hypoacousia' is unrelated to the study drug bosutinib. The event is not consistent with the known drug safety profile and occurred more than 21 months after the last dose of bosutinib was administered.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2019 to 2019	Relevant Med History	Carotid artery occlusion (Carotid artery occlusion);
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		74 Years	Male	Unk	06	JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

BILATERAL PLEURAL EFFUSION [Pleural effusion]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) for protocol B1871047.

A 74 year-old male patient received bosutinib (BOSULIF), from

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) SPRYCEL (DASATINIB MONOHYDRATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2) UNK	#2) Unknown

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) 07-NOV-2019 / 03-DEC-2019	#1) 27 days
#2) 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
2011 to 2011	Relevant Med History OPERTAED	Abdominal aortic aneurysm (Aortic aneurysm)
Unknown	Relevant Med History	Aortic aneurysm repair (Aortic aneurysm repair)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391902

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

07Nov2019 (Batch/Lot number: unknown) to 03Dec2019 at 500 mg 1x/day; dasatinib monohydrate (SPRYCEL) (Batch/Lot number: unknown). Relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011, notes: OPERTAED; "OPERTAED ABDOMINAL AORTIC ANEURYSM" (unspecified if ongoing); "CLOGGED LEFT INTERNAL CAROTID", start date: 2019, stop date: 2019, notes: ENDARTERECTOMY; "ENDARTERECTOMY" (unspecified if ongoing). The patient's concomitant medications were not reported.
The following information was reported: PLEURAL EFFUSION (hospitalization) with onset 06Jun2020, outcome "recovered" (27Jun2020), described as "BILATERAL PLEURAL EFFUSION". The patient was hospitalized for pleural effusion (start date: 20Jun2020, discharge date: 27Jun2020, hospitalization duration: 7 day(s)). The patient underwent the following laboratory tests and procedures: chest x-ray: satisfactory chest x-ray control, notes: satisfactory chest x-ray control: almost complete disappearance of the right effusion and persistence of a blunting of the left pleural recesses. The action taken for bosutinib was reported as post-therapy. The action taken for dasatinib monohydrate was temporarily withdrawn. Therapeutic measures were taken as a result of pleural effusion.

The investigator considered there was not a reasonable possibility that the event "bilateral pleural effusion" was related to bosutinib.

Additional information: event grade 3. the patient was hospitalized from 20Jun2020 to 27Jun2020 for treatment of bilateral pleural effusion. 2 evacuation punctures. According to the investigator, the event was unrelated to the study drug bosutinib but related to concomitant drug SPRYCEL.The cause of pleural effusion is most likely related to its treatment with SPRYCEL from its CML. suspension of SPRYCEL and patient is put on LASILIX at 40 mg. The patient returns home on 27Jun2020 after satisfactory chest x-ray control: almost complete disappearance of the right effusion and persistence of a blunting of the left pleural recesses.

Case Comment: In concurrence with the investigator, the reported pleural effusion is unrelated to the study drug bosutinib. Of note, the event occurred more than 6 months after the last dose of bosutinib was administered. The patient's other medication may provide an alternative explanation for the event.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Chest X-ray	satisfactory chest x-ray control	
		satisfactory chest x-ray control: almost complete disappearance of the right effusion and persistence of a blunting of the left pleural recesses.		

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
2019 to 2019	Relevant Med History ENDARTERECTOMY	Carotid artery occlusion (Carotid artery occlusion);
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		74 Years	Male	Unk	14	JAN	2021

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

EXERTIONAL DYSPNEA [Dyspnoea exertional]
PERIORBITAL OEDEMAS [Periorbital oedema]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) GLIVEC (IMATINIB MESILATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2) UNK	#2) Unknown

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) 07-NOV-2019 / 03-DEC-2019	#1) 27 days
#2) 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
2011 to 2011	Relevant Med History operated	Abdominal aortic aneurysm (Aortic aneurysm)
2019 to 2019	Relevant Med History ENDARTERECTOMY	Carotid artery occlusion (Carotid artery occlusion)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391956

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
09-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200391956

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 74-year-old male patient received bosutinib (BOSULIF), from 07Nov2019 to 03Dec2019 at 500 mg 1x/day; imatinib mesilate (GLIVEC), (Batch/Lot number: unknown). The patient's relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011, notes: operated; "LEFT INTERNAL CAROTID ARTERY BLOCKED", start date: 2019, stop date: 2019, notes: ENDARTERECTOMY; "ENDARTERECTOMY" (unspecified if ongoing). The patient's concomitant medications were not reported.
The following information was reported: DYSPNOEA EXERTIONAL (non-serious) with onset 14Jan2021, outcome "recovered" (08Apr2021), described as "EXERTIONAL DYSPNEA"; PERIORBITAL OEDEMA (non-serious) with onset 14Jan2021, outcome "recovered" (08Apr2021), described as "PERIORBITAL OEDEMAS". The action taken for bosutinib was unknown; for imatinib mesilate was dosage not changed.
Additional information: events exertional dyspnea and periorbital oedemas were non-serious, grade 1. The investigator considered that events were unrelated to bosutinib and related to concomitant drug GLIVEC. The site described: the patient presented during the consultation of 14Jan2021 an exertional dyspnea and periorbital oedemas. No additional concomitant treatments or modification of current treatment for these adverse events.

The reporter considered "exertional dyspnea" and "periorbital oedemas" not related to bosutinib.

No follow-up attempts are possible. No further information is expected.

Case Comment: In concurrence with the investigator, the reported exertional dyspnea and periorbital oedemas are unrelated to the administration of bosutinib. The events occurred more than 1 year after the last dose of bosutinib. The patient's other medication may provide an explanation for the events.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		75 Years	Male	Unk	06	MAY	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ASTHENIA [Asthenia]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet
#2) GLIVEC (IMATINIB MESILATE)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2) UNK	#2) Unknown

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) 07-NOV-2019 / 03-DEC-2019	#1) 27 days
#2) 31-JUL-2020 / Ongoing	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SPRYCEL (DASATINIB MONOHYDRATE) ; 15-JAN-2020 / 22-JUN-2020

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 2011	Relevant Med History operated	Abdominal aortic aneurysm (Aortic aneurysm)
2019 to 2019	Relevant Med History ENDARTERECTOMY	Carotid artery occlusion (Carotid artery occlusion)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200391990

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
25-APR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: 202200391990

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), from 07Nov2019 to 03Dec2019 at 500 mg 1x/day; imatinib mesilate (GLIVEC), since 31Jul2020 (ongoing) (Batch/Lot number: unknown). The patient's relevant medical history included: "ABDOMINAL AORTIC ANEURYSM", start date: 2011, stop date: 2011, notes: operated; "LEFT INTERNAL CAROTID ARTERY BLOCKED", start date: 2019, stop date: 2019, notes: ENDARTERECTOMY; "ENDARTERECTOMY" (unspecified if ongoing). Concomitant medication(s) included: SPRYCEL, start date: 15Jan2020, stop date: 22Jun2020.
The following information was reported: ASTHENIA (non-serious) with onset 06May2020, outcome "not recovered". The action taken for bosutinib was unknown; for imatinib mesilate was dosage not changed.
Asthenia was documented as chronic since 05Jul2021. Asthenia was rated grade 1.

The reporter considered "asthenia" not related to bosutinib and related to concomitant drug GLIVEC.

No follow-up attempts are possible. No further information is expected.

Follow-up (25Apr2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

Updated information includes: updated event verbatim (from Chronic asthenia to Asthenia), updated event onset date (from 05Jul2021 to 06May2020), concomitant medication (SPRYCEL), start date and ongoing therapy status for GLIVEC.

Case Comment: In concurrence with the reporter, the reported asthenia is unrelated to the study drug bosutinib. The patient's other medication may provide an explanation for the event.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown	Relevant Med History	Endarterectomy (Endarterectomy);

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	FRANCE		PRIVACY		79 Years	Female	58.00 kg	22	AUG	2018

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Diffuse pain [Pain]

Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047.

(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) Bosutinib (BOSUTINIB) Unknown

15. DAILY DOSE(S)
#1) 500 mg, 1x/day

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 19-APR-2016 / 25-APR-2016

19. THERAPY DURATION
#1) 7 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	None ()

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200400652

24c. DATE RECEIVED BY MANUFACTURER
10-MAR-2022

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 79-year-old female patient (unknown if pregnant) received bosutinib (BOSUTINIB), from 19Apr2016 to 25Apr2016 at 500 mg 1x/day. The patient had no relevant medical history. The patient's concomitant medications were not reported. The following information was reported: PAIN (non-serious) with onset 22Aug2018, outcome "recovered" (22Nov2018), described as "Diffuse pain".

Additional information: The event 'diffuse pain' was rated grade 1. The patient complained of diffuse pain during the consultation on 22Aug2018. The patient has then been on therapeutic abstention for 5 months. These pains are not described during the following consultation on 22Nov2018.

The reporter considered "diffuse pain" not related to bosutinib.

Case Comment: Based on the information currently available, there is not a reasonable possibility that the event "Diffuse pain" is related to the suspect drug, but most likely represents patient intercurrent medical condition.

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	FRANCE		PRIVACY		74 Years	Male	Unk	19	JUN	2020

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

branch occlusion retinal vein occlusion eye right [Retinal vein occlusion]
Hypertension [Hypertension]

Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE

This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.

(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) Bosulif (BOSUTINIB) Film-coated tablet

15. DAILY DOSE(S)
#1) 500 mg, daily

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Unknown

18. THERAPY DATES(from/to)
#1) 07-NOV-2019 / 03-DEC-2019

19. THERAPY DURATION
#1) 27 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) GLIVEC (IMATINIB MESILATE) ; 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	Type 2 diabetes mellitus (Type 2 diabetes mellitus)
Unknown	Relevant Med History	Cataract (Cataract)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
Stella Pietrafesa
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New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
202200414902

24c. DATE RECEIVED BY MANUFACTURER
25-APR-2023

24d. REPORT SOURCE
☒ STUDY ☐ LITERATURE
☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
27-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: 202200414902

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 74-year-old male patient received bosutinib (BOSULIF), from 07Nov2019 to 03Dec2019 at 500 mg daily. The patient's relevant medical history included: "diabetes type 2" (ongoing); "Cataract" (unspecified if ongoing); "AMD" (ongoing); "Glaucoma" (ongoing). Concomitant medication(s) included: GLIVEC.
The following information was reported: HYPERTENSION (non-serious) with onset 19Jun2020, outcome "recovered" (20Jun2020); RETINAL VEIN OCCLUSION (hospitalization) with onset 15Jul2021, outcome "recovered" (01Feb2022), described as "branch occlusion retinal vein occlusion eye right". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of retinal vein occlusion.

Clinical course: Vitrectomy done in ambulatory. On 25Apr2023, was reported intravitreal hemorrhage due to occlusion of retinal vein branch occlusion complicated by a macroaneurysm plus non vascular glaucoma glaucoma (history) stage I with iridial rubeosis in the iridocrone angle and proliferative diabetic retinopathy without ocular hypertonia (history of T2D). 1st intervention 09Nov2021 surgery (ambulatory) by vitrectomy plus retinal panphotocoagulation operative follow-up marked by massive recurrence of intravitreal hemorrhage, with no spontaneous favorable evolution. 2nd operation (ambulatory) 01Feb2022 additional dissection of the neovascular veils of retinal panphotocoagulation and placement of silicone oil. Favorable outcome.
The event retinal vein occlusion was rated grade 3 serious due to hospitalization, and hypertension was rated grade 3 non-serious.

The reporter considered "branch occlusion retinal vein occlusion eye right" and "hypertension" not related to bosutinib or to any concomitant drug.

Follow-up (21Mar2022). This follow-up is received from the investigational site via CRO. Updated information included: recovery date of event hypertension was 20Jun2020 (not 20Jun2021).

Follow-up (25Apr2023): This is a follow-up non-interventional study report (Post Authorization Safety Study) received from the investigational site via the CRO for protocol B1871047.
Updated information included: reporter details, RMH, event 'Vitreous haemorrhage' recoded to 'Retinal vein occlusion', outcome, seriousness and clinical course.

Case Comment: Based on the information available, the reported branch occlusion retinal vein occlusion eye right and hypertension are unrelated to the study drug bosutinib. The events occurred more than 6 months after the last dose of bosutinib was administered.

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	Age-related macular degeneration (Age-related macular degeneration);
Unknown to Ongoing	Relevant Med History	Glaucoma (Glaucoma);