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		57 Years	Female	86.00 kg		NOV	2016

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

left lobe steatotic hepatomegaly [Hepatomegaly]

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 57-year-old female 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) 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.
PV202300036123

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

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

DATE OF THIS REPORT
28-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

The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: HEPATOMEGALY (non-serious) with onset Nov2016, outcome "unknown", described as "left lobe steatotic hepatomegaly".

The reporter considered "left lobe steatotic hepatomegaly" not related to bosutinib.

Additional information: Relevant medical history, concomitant drug and relevant test were not reported. The event was rated non-serious with grade 1. The event was unrelated to the study drug BOSULIF and unrelated to concomitant drug.

Case Comment: The limited information provided precludes a full clinical assessment of the case. Based on the information currently available, with medical history, concomitant medications, relevant laboratory data and course of event unknown at the time of this report, and in concurrence with reporting healthcare professional, the Company considers there is not enough evidence to attribute the reported "left lobe steatotic hepatomegaly" to study drug bosutinib. Event is possibly an intercurrent medical condition. This case will be reassessed once with additional information.

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	Female	Unk		NOV	2018

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

Asthenia [Asthenia]
Hot flashes [Hot flush]

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 (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) SPRYCEL (DASATINIB MONOHYDRATE)

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

15. DAILY DOSE(S)
#1)
#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) Unknown
#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.
PV202300036698

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 54-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF); dasatinib monohydrate (SPRYCEL), (Batch/Lot number: unknown). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ASTHENIA (non-serious) with onset Nov2018, outcome 'recovered' (Nov2018); HOT FLUSH (non-serious) with onset Nov2018, outcome 'recovered' (Nov2018), described as 'Hot flashes'. The action taken for bosutinib was unknown. The action taken for dasatinib monohydrate was temporarily withdrawn.
Additional information: unrelated to study drug and related to concomitant treatment SPRYCEL that was temporarily withdrawn.

The reporter considered 'asthenia' and 'hot flashes' not related to bosutinib.

Case Comment: Considering the known product safety profile, a causal association between the study drug bosutinib and the reported 'asthenia' cannot be completely excluded. The reported 'hot flashes' likely represents an intercurrent condition 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		71 Years	Male	95.00 kg		FEB	2020

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

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

(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) JUN-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.
PV202300040819

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

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
31-MAR-2023

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 71-year-old male patient received bosutinib (BOSULIF), first regimen since Jun2019 at 100 mg daily, second regimen since Jul2019 at 100 mg, third regimen since 15Oct2019 at 200 mg and fourth regimen since 22Oct2019 at 300 mg.
The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DYSPNOEA (non-serious) with onset Feb2020, outcome "not recovered", described as "dyspnea". The action taken for bosutinib was dose not changed.

The reporter considered "dyspnea" related to bosutinib.

Additional information: it was also reported that patient experienced loss of response on 05Nov2019 resolved on 07Jan2020 (not reportable). It was rated grade 2. The event was assessed as related to bosulif and unrelated to any concomitant drug. Then patient experienced the event dyspnea that was rated grade 2. Bosutinib dose was increased in order to obtain response to cancer as follows: bosutinib at 100 mg in Jul2019, 200 mg on 15Oct2019 and 300 mg on 22Oct2019. There was no reduction dose due to dyspnea. Action taken in response to such event was dose not changed. The event was reported as non-serious.

Follow-up (23Mar2023): 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: EDENTES reported in concomitant section was deleted, details on action taken with bosutinib (Bosutinib dose was increased in order to obtain response to cancer, no reduction dose due to dyspnea).

Follow-up (31Mar2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) for protocol B1871047. Updated information: action taken updated to dose not changed.

Case Comment: Based on a temporal association and known product safety profile, dyspnea is 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	100 mg; Unknown	Unknown	JUL-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg; Unknown	Unknown	15-OCT-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	300 mg; Unknown	Unknown	22-OCT-2019 / 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		64 Years	Male	81.00 kg		OCT	2020

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

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 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) 08-SEP-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.
PV202300052654

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

24c. DATE RECEIVED BY MANUFACTURER
17-MAR-2023

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 64-year-old male patient received bosutinib (BOSULIF), since 08Sep2017 (ongoing) at 400 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DYSPNOEA (non-serious) with onset Oct2020, outcome "not recovered", described as "Dyspnea". The action taken for bosutinib was dosage not changed.
Event Dyspnea was considered as non-serious and rated grade 1.
The reporter considered "dyspnea" not related to bosutinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the information currently available (and in concurrence with reporting physician), although consistent with known product safety profile of bosutinib, the reported 'dyspnea' occurred three years after initial administration of study drug and is considered 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		69 Years	Male	60.00 kg		AUG	2018

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

depressive syndrome [Depression]

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) 03-MAY-2018 / 24-MAY-2018

19. THERAPY DURATION
#1) 22 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.
PV202300055947

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

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

DATE OF THIS REPORT
28-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 69-year-old male patient received bosutinib (BOSULIF), from 03May2018 to 24May2018 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: DEPRESSION (non-serious) with onset Aug2018, outcome "not recovered", described as "depressive syndrome". Therapeutic measures were taken as a result of depression.

The reporter considered "depressive syndrome" not related to bosutinib.

Additional information: The event Depressive syndrome was rated grade 2. Event reported as non-serious. Initiation of an antidepressant and anxiolytic treatment (improvement, appetite recovery). The investigator considered that the event was unrelated to bosutinib and unrelated to any concomitant medication.

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

Case Comment: In concurrence with the investigator, based on the available information, the event "depressive syndrome" was most likely related to the patient's underlying condition and assessed as unrelated to the study drug 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		70 Years	Male	60.00 kg	30	OCT	2018

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

Right knee wound [Joint injury]

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) 03-MAY-2018 / 24-MAY-2018

19. THERAPY DURATION
#1) 22 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	Limb prosthesis user (Limb prosthesis user)

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.
PV202300055952

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 03May2018 to 24May2018 at 300 mg daily. The patient's relevant medical history included: "right lower limb prosthesis" (unspecified if ongoing). The patient's concomitant medications were not reported.
The following information was reported: JOINT INJURY (non-serious) with onset 30Oct2018, outcome "not recovered", described as "Right knee wound".

Additional information: right leg prosthesis too tight (repeated trauma). The event right knee wound was rated grade 2. Event reported as non-serious.

The reporter considered "right knee wound" not related to bosutinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: The company concurs with the reporter and consider ""right knee wound" an intercurrent condition and not related 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		64 Years	Male	Unk		MAR	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
severe hypocalcemia [Hypocalcaemia]

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) 23-MAY-2019 / 26-MAR-2020

19. THERAPY DURATION
#1) 10 months 4 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.
PV202300055953

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

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

DATE OF THIS REPORT
28-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 64-year-old male patient received bosutinib (BOSULIF), from 23May2019 to 26Mar2020. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: HYPOCALCAEMIA (medically significant) with onset Mar2020, outcome "recovered" (Mar2020), described as "severe hypocalcemia". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of hypocalcaemia.
The serious grade of event was 3. Occurrence during hospitalization from 22Mar2020 to 17Apr2020 due to pneumopathy, vitamin D treatment, intravenous supplementation. The hospitalization occurred while the patient was still treated with bosutinib (discontinuation of bosutinib on 26Mar2020).

The investigator considered there's no reasonable probability that the event is linked to the studied medicine or concomitant medicine.

Follow-up (17Apr2023): This is a non-interventional study follow up report received from the Clinical team for protocol B1871047. Updated information: bosutinib stop date, clinical course.

Follow-up (25Jul2023). This follow-up is received from the clinical team following the query:

Bosulif was started on 23May2019. Seriousness criteria for the event severe hypocalcemia confirmed as medically significant. Hospitalisation for pneumopathy reported in related case.

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

Case Comment: Based on the information available, the event hypocalcemia is unrelated to bosutinib. The event is most likely an intercurrent condition. Of note, the event resolved without any modification in 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		69 Years	Male	60.00 kg		JUL	2018

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

constipation [Constipation]

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) 03-MAY-2018 / 24-MAY-2018

19. THERAPY DURATION
#1) 22 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.
PV202300055971

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

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

DATE OF THIS REPORT
28-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 69-year-old male patient received bosutinib (BOSULIF), from 03May2018 to 24May2018 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: CONSTIPATION (non-serious) with onset Jul2018, outcome "recovered" (10Aug2018).

The reporter considered "constipation" not related to bosutinib.

Additional information: The event Constipation was rated grade 2. Event reported as non-serious. The investigator considered that the event was unrelated to bosutinib and unrelated to any concomitant medication.

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

Case Comment: Available information is limited. Last dose of bosutinib was reported on 24May2018, over a month before event onset date. The company concurs with the reporter that reported "constipation" is unrelated to bosutinib but more likely an intercurrent medical condition in this elderly 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		70 Years	Male	60.00 kg	15	FEB	2019

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

Other Serious Criteria: Medically Significant
Acid folic deficiency [Folate 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, daily

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

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

18. THERAPY DATES(from/to)
#1) 03-MAY-2018 / 04-JUN-2018

19. THERAPY DURATION
#1) 1 month 2 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.
PV202300056903

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 70-year-old male patient received bosutinib (BOSULIF), from 03May2018 to 04Jun2018 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: FOLATE DEFICIENCY (medically significant) with onset 15Feb2019, outcome "recovering", described as "Acid folic deficiency".
Event was grade 3, event medically significant as it probably slows down recovery, see medullary necrosis in the context of severe denutrition.

The reporter considered "acid folic deficiency" not related to bosutinib.

Case Comment: The company concurs with the reporter that "acid folic deficiency" is unrelated to bosutinib. To be noted, last dose of bosutinib was reported on 04Jun2018, over 8 months before event onset date of 15Feb2019.

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	Male	60.00 kg	21	FEB	2019

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

Pancytopenia [Pancytopenia]
Repeated malaises [Malaise]

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) HYDREA (HYDROXYCARBAMIDE)
(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) 300 mg, daily	#1) Unknown
#2) 2 DF, daily	#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) 02-MAR-2018 / 24-MAY-2018	#1) 2 months 23 days
#2) 10-AUG-2018 / 16-AUG-2018	#2) 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	Relevant Med History since 20-year-old	Penicillin allergy (Drug hypersensitivity)

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.
PV202300056961

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 02Mar2018 to 24May2018 at 300 mg daily; hydroxycarbamide (HYDREA), first regimen from 10Aug2018 (Batch/Lot number: unknown) to 16Aug2018 at 2 DF daily, second regimen from 16Aug2018 (Batch/Lot number: unknown) to 22Nov2018 at 1 DF daily, third regimen from 22Nov2018 (Batch/Lot number: unknown) to 29Dec2018 at 2 DF daily and fourth regimen since 29Dec2018 (Batch/Lot number: unknown) at 3 DF daily. The patient's relevant medical history included: "Penicillin allergy" (unspecified if ongoing), notes: since 20-year-old. The patient's concomitant medications were not reported.
The following information was reported: PANCYTOPENIA (hospitalization, life threatening) with onset 21Feb2019, outcome "not recovered"; MALAISE (hospitalization) with onset 26Feb2019, outcome "not recovered", described as "Repeated malaises". The action taken for hydroxycarbamide was dosage reduced. The following death information was reported, despite no fatal outcome. The patient date of death was unknown. Reported cause of death: "alteration of general status with cachexia and negligence".

The investigator considered that pancytopenia was unrelated to bosutinib and related to HYDREA and that repeated malaises was unrelated to bosutinib or to any concomitant drug.

Pancytopenia, 3 possible main origins. Possible toxicity to hydroxycarbamide (HYDREA) as there was neither blast nor neutropenia on complete blood count. The patient started to receive HYDREA on 10Aug2018 (2 tablets/day) then decreased on 16Aug2018 at 1 tablet/day increased again at 2 tablets/day on 22Nov2018 by the physician then 3 tablet/day on 29Dec2018. In the middle of Jan2019 the dosage increased gradually until 6 tablets/day, intentional overdose? The patient reported that he probably made a mistake in HYDREA intake but not an intentional overdose. HYDREA dose reduced to 5 tablets at the time of hospitalization in nephrology department. Event pancytopenia was considered as related to concomitant medication HYDREA. In response to the event pancytopenia, HYDREA dose was reduced. Second origin possibility: AUGMENTIN toxicity started a few days before hospitalization for bronchitis and continued until until 20Feb2019 (48h after toe amputation), however the patient was considered allergic to penicillin since the age of 20 years and third possibility: folic acid deficiency disclosed on 15Feb2019. Event "repeated malaises" with malaise on 26Feb2019, slight malaise on 01Mar2019, malaise in the bathroom on 02Mar2019. Malaise after hemodialysis session, with patient's death quickly after due to alteration of general status with cachexia and negligence. Event repeated malaise was rated grade 4 (instead of 5).

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

Follow-up (29Mar2023): This is a follow-up to a non-interventional study for protocol B1871047.
Updated information included: HYDREA updated to Suspect-concomitant medication, action taken for bosutinib updated to not applicable, causality assessment for pancytopenia related to HYDREA, event verbatim for malaise updated to "repeated malaises", seriousness updated to grade 4, cause of death updated.

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

Follow-up (16Apr2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from a contactable reporter (Physician) from the investigational site via the CRO for protocol B1871047.
Updated information includes: Onset date of event "repeated malaises" changed from 02Mar2019 to 26Feb2019.

Case Comment: The events malaise and pancytopenia are unrelated to bosutinib. The temporal relationship is not plausible. 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
#2) HYDREA (HYDROXYCARBAMIDE) ; Regimen #2	1 DF, daily; Unknown	Unknown	16-AUG-2018 / 22-NOV-2018; 3 months 7 days
#2) HYDREA (HYDROXYCARBAMIDE) ; Regimen #3	2 DF, daily; Unknown	Unknown	22-NOV-2018 / 29-DEC-2018; 1 month 8 days
#2) HYDREA (HYDROXYCARBAMIDE) ; Regimen #4	3 DF, daily; Unknown	Unknown	29-DEC-2018 / Unknown;

Mfr. Control Number: PV202300056961

ADDITIONAL INFORMATION

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
			Unknown

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	60.00 kg	03	MAY	2018

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

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) 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) 03-MAY-2018 / 24-MAY-2018

19. THERAPY DURATION
#1) 22 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) ERYTHROPOIETIN (ERYTHROPOIETIN) ; 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.
PV202300056971

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

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

DATE OF THIS REPORT
28-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 69-year-old male patient received bosutinib (BOSULIF), from 03May2018 to 24May2018 at 300 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: ERYTHROPOIETIN.
The following information was reported: ANAEMIA (non-serious) with onset 03May2018, outcome "recovered" (2018), described as "anemia". Therapeutic measures were taken as a result of anaemia.
The reporter considered "anemia" not related to bosutinib.

Additional information: Remote anemia from blood loss following accidental disconnection during a dialysis at the beginning of May2018, the patient was still anemic as on 24May20218, increase in EPO dose. Event Anemia was assessed as grade 2, non-serious. The event is reported as unrelated to any concomitant drug.

Case Comment: Event "anemia" with reported onset date on 03May2018, the same date when bosutinib started, is considered unrelated to bosutinib but related to the medical condition that needed dialysis and mentioned blood loss during the dialysis.

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		69 Years	Male	60.00 kg	01	FEB	2018

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

Recurring bullous eruption [Dermatitis bullous]

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) UNK	#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) 21-SEP-2017 / 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	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.
PV202300056978

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 69-year-old male patient received bosutinib (BOSULIF), first regimen since 21Sep2017 and second regimen from 28Dec2017 to 01Feb2018 at 400 mg daily. The patient had no relevant medical history. The patient's concomitant medications were not reported. The following information was reported: DERMATITIS BULLOUS (non-serious) with onset 01Feb2018, outcome "recovered" (2018), described as "recurring bullous eruption". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of dermatitis bullous.

The reporter considered "recurring bullous eruption" not related to bosutinib.

Additional information: The event was rated grade 2, non-serious. Treatment for the event: fatty cream application. Reporter comment: The patient decided to withdraw the treatment on 01Feb2018. Bosutinib resumed on 15Feb2018 (investigator decision). The investigator considered that the event was unrelated to any concomitant drug.

Follow-up (14Apr2023): This is a non-interventional study follow-up report from CRO for protocol B1871047.
Updated information included: updated bosutinib therapy dates, updated event onset date, reporter comment.

Follow-up (25Jul2023): 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: suspect product data (start date), confirmation of event onset date and causality assessment.

Case Comment: Based on available information, "recurring bullous eruption" is considered unrelated to bosutinib. To be noted, the patient decided to withdraw the treatment on 01Feb2018, and action taken for bosutinib was dosage not changed.

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, daily; Unknown	Unknown	28-DEC-2017 / 01-FEB-2018; 1 month 5 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		70 Years	Male	60.00 kg		FEB	2019

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

renutrition syndrome [Refeeding syndrome]
Oral mycosis [Oral fungal 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) 300 mg, daily

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

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

18. THERAPY DATES(from/to)
#1) 02-MAR-2018 / 24-MAY-2018

19. THERAPY DURATION
#1) 2 months 23 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.
PV202300056983

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 02Mar2018 to 24May2018 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ORAL FUNGAL INFECTION (non-serious) with onset Feb2019, outcome "unknown", described as "Oral mycosis"; REFEEDING SYNDROME (non-serious) with onset 26Feb2019, outcome "recovered" (01Mar2019), described as "renutrition syndrome".
The reporter considered "renutrition syndrome" and "oral mycosis" not related to bosutinib.

Additional information: The patient requests to implement enteral nutrition implementation of a naso-gastic tube on 26Feb2019. Beginning of enteral feeding complicated with inappropriate renutrition syndrome requiring stop. Per os supply resumed on 01Mar2019. The events Refeeding syndrome and Stomatomycosis were rated grade 2, non-serious. The investigator considered that the events were unrelated to any concomitant drug.

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

Case Comment: Based on the available information and the lack of drug-event temporal relationship, the events oral mycosis and renutrition syndrome are considered in agreement with the reporter as 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		64 Years	Male	Unk	10	AUG	2021

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

Lymphopenia [Lymphopenia]
Tinnitus [Tinnitus]

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) 04-JUN-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.
PV202300075048

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

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

DATE OF THIS REPORT
28-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 64-year-old male patient received bosutinib (BOSULIF), since 04Jun2019 (ongoing) at 300 mg 1x/day. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: LYMPHOPENIA (non-serious) with onset 10Aug2021, outcome "recovered" (01Feb2022); TINNITUS (non-serious) with onset 2022, outcome "not recovered". The event Lymphopenia was rated grade 1 and reported as non-serious. The event Tinnitus was rated grade 2 and reported as non-serious. It was reported non-permanent tinnitus, ENT consultation, proposed apparatus. The action taken for bosutinib was dosage not changed.

The investigator considered that the event Lymphopenia was related to bosutinib and unrelated to any concomitant drug. The investigator considered that the event tinnitus was unrelated to bosutinib or to any concomitant drug.

Case Comment: Based on the available information, the company considers that a causal relationship between lymphopenia and bosutinib cannot be excluded due to plausible temporal association. The Company considers the reported event tinnitus 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 Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	FRANCE		PRIVACY		Unk	Male	92.00 kg		NOV	2018

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

Pulmonary arterial hypertension [Pulmonary arterial 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) 300 mg, 1x/day

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

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

18. THERAPY DATES(from/to)
#1) 30-JUN-2016 / 21-JUN-2017

19. THERAPY DURATION
#1) 11 months 23 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) ; 10-JUL-2017 / 09-NOV-2018
#2) IMATINIB (IMATINIB) ; 28-NOV-2018 / 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.
PV202300075925

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 30Jun2016 to 21Jun2017 at 300 mg 1x/day. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: SPRYCEL oral taken for chronic myeloid leukaemia, start date: 10Jul2017, stop date: 09Nov2018; IMATINIB oral taken for chronic myeloid leukaemia, start date: 28Nov2018 (ongoing).
The following information was reported: PULMONARY ARTERIAL HYPERTENSION (hospitalization) with onset Nov2018, outcome "recovered" (19Feb2019). Therapeutic measures were taken as a result of pulmonary arterial hypertension.

The reporter considered "pulmonary arterial hypertension" not related to bosutinib.

Additional information: Investigator's verbatim narrative: catheterism right on 23Nov2018. taken cognizance by tec on 25Apr2023. The event Pulmonary arterial hypertension was rated grade 3. The investigator considered that the event was unrelated to bosutinib or to any concomitant drug.

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

Case Comment: Based on the available information, the Company considers the reported event pulmonary arterial hypertension is unrelated to suspect drug bosutinib. The event occurred 1 year 4 months after 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		48 Years	Male	92.00 kg		OCT	2018

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

Bilateral pleural effusion, predominating on the right [Pleural effusion]
Pulmonary decompensation [Respiratory failure]
Infectious episode [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 received from contactable reporter (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) SPRYCEL (DASATINIB MONOHYDRATE)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 300 mg, daily	#1) Unknown
#2) UNK	#2) Oral

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 30-JUN-2016 / 21-JUN-2017	#1) 11 months 23 days
#2) 10-JUL-2017 / 09-NOV-2018	#2) 1 year 4 months

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 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.
PV202300075926

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 30Jun2016 to 21Jun2017 at 300 mg daily; dasatinib monohydrate (SPRYCEL), from 10Jul2017 (Batch/Lot number: unknown) to 09Nov2018, oral for chronic myeloid leukaemia. The patient's relevant medical history included: 'Chronic myelogenous leukemia' (ongoing). The patient's concomitant medications were not reported.
The following information was reported: INFECTION (non-serious) with onset Oct2018, outcome "recovered" (Nov2018), described as "Infectious episode"; PLEURAL EFFUSION (hospitalization) with onset 23Oct2018, outcome "recovered" (21Nov2018), described as "Bilateral pleural effusion, predominating on the right"; RESPIRATORY FAILURE (hospitalization) with onset 09Nov2018, outcome "recovered" (19Feb2019), described as "Pulmonary decompensation". The patient was hospitalized for pleural effusion, respiratory failure (start date: 09Nov2018, discharge date: 21Nov2018, hospitalization duration: 13 day(s)). The action taken for dasatinib monohydrate was dosage permanently withdrawn on 09Nov2018. Action taken for bosutinib was reported as Not applicable.

The reporter considered 'bilateral pleural effusion, predominating on the right', 'pulmonary decompensation' and "infectious episode" not related to bosutinib. The reporter considered 'bilateral pleural effusion, predominating on the right' related to concomitant drug Sprycel.

Follow-up (15Sep2023): This is a non-interventional study follow-up report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information: new event (Infectious episode).

Case Comment: Based on the available information, the Company considers the reported events 'bilateral pleural effusion, predominating on the right', 'pulmonary decompensation' and 'infectious episode' are unrelated to suspect drug bosutinib. The events occurred more than 1 year after last dose of bosutinib. The events are more likely related to Sprycel.

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	Male	92.00 kg			2019

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

Alveolar hypoventilation [Hypoventilation]
sleep apnea syndrome [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 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) 30-JUN-2016 / 21-JUN-2017

19. THERAPY DURATION
#1) 11 months 23 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) IMATINIB (IMATINIB) ; 28-NOV-2018 / 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 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.
PV202300075928

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), from 30Jun2016 to 21Jun2017 at 300 mg daily. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). Concomitant medication(s) included: IMATINIB oral, start date: 28Nov2018 (ongoing).
The following information was reported: HYPOVENTILATION (hospitalization) with onset 2019, outcome "not recovered", described as "Alveolar hypoventilation"; SLEEP APNOEA SYNDROME (hospitalization) with onset 2019, outcome "not recovered", described as "sleep apnea syndrome". The patient was hospitalized for hypoventilation, sleep apnoea syndrome (start date: 02May2019, discharge date: 03May2019, hospitalization duration: 2 day(s)). Therapeutic measures were taken as a result of sleep apnoea syndrome.

The reporter considered "alveolar hypoventilation" and "sleep apnea syndrome" not related to bosutinib or any concomitant drug.

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

Case Comment: Based on the available information, the Company considers the reported events "alveolar hypoventilation" and "sleep apnea syndrome" are unrelated to suspect drug bosutinib. Both events occurred more than 1 year 6 months after 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		78 Years	Female	52.00 kg	06	MAR	2023

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

cardiomegaly [Cardiomegaly]
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 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/ 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) 31-MAR-2022 / 30-JUN-2022

19. THERAPY DURATION
#1) 3 months

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) DASATINIB (DASATINIB) ; 01-JUL-2022 / 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.
PV202300084633

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old female patient received bosutinib (BOSULIF), from 31Mar2022 to 30Jun2022 at 300 mg/ 200 mg alternately for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: DASATINIB oral taken for chronic myeloid leukaemia, start date: 01Jul2022 (ongoing).
The following information was reported: CARDIOMEGALY (non-serious) with onset 06Mar2023, outcome "not recovered"; DYSPNOEA (non-serious) with onset 06Mar2023, outcome "not recovered", described as "dyspnea".

The reporter considered "cardiomegaly" and "dyspnea" not related to bosutinib.

Additional information: Both events were rated grade 1. According to the investigator, both events were unrelated to concomitant drug.
Follow-up attempts are completed. No further information is expected.

Follow-up (18Jul2023): This is a non-interventional follow-up study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.

Updated information includes: updated start date of bosutinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: Events represent intercurrent medical conditions 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		78 Years	Female	52.10 kg	14	FEB	2023

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

flu syndrom [Influenza]
lower limb edema [Oedema peripheral]

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 / 200 mg alternately

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

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

18. THERAPY DATES(from/to)
#1) 30-JUN-2022 / 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) DASATINIB (DASATINIB) ; 01-JUL-2022 / 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.
PV202300084637

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old female patient received bosutinib (BOSULIF), since 30Jun2022 at 300 mg / 200 mg alternately. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: DASATINIB oral taken for chronic myeloid leukaemia, start date: 01Jul2022 (ongoing).
The following information was reported: INFLUENZA (non-serious) with onset 14Feb2023, outcome "recovering", described as "flu syndrom"; OEDEMA PERIPHERAL (non-serious) with onset Mar2023, outcome "recovered" (07Mar2023), described as "lower limb edema".

The reporter considered "flu syndrom" and "lower limb edema" not related to bosutinib.

Additional information: Flu syndrome was rated grade 2. Lower limb edema was rated grade 1. The action taken in response to the events for dasatinib was dose not changed. According to the investigator, both events were unrelated to bosutinib and concomitant drug.

Follow-up attempts are not needed. No further information is expected.

Case Comment: Based on the available information, the Company considers the reported events "flu syndrome" and "lower limb edema" are unrelated to suspect drug bosutinib but more likely inter-current 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		60 Years	Male	104.00 kg			2020

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

cervical and peri-axillary pendulum [Acrochordon]

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) 11-MAY-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
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.
PV202300084640

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 60-year-old male patient received bosutinib (BOSULIF), since 11May2018 (ongoing) at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: ACROCHORDON (non-serious) with onset 2020, outcome "recovered" (2020), described as "cervical and peri-axillary pendulum". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of acrochordon.

Additional information: resection was performed on 14Aug2020 + cryotherapy/liquid azote.

The reporter considered "cervical and peri-axillary pendulum" not related to bosutinib. Event unrelated to concomitant treatments.

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

Follow-up (17Jul2023): 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: bosutinib start date.

Case Comment: Based on the available information, the Company considers the reported event cervical and peri-axillary pendulum 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 Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	FRANCE		PRIVACY		78 Years	Female	52.10 kg			2022

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

HIATAL HERNIA [Hiatus hernia]
Pericardial effusion [Pericardial 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
#2) DASATINIB (DASATINIB)
(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) 300 mg, daily	#1) Unknown
#2) UNK	#2) Oral

17. INDICATION(S) FOR USE
#1) Unknown
#2) CML (Chronic myeloid leukaemia)

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 08-APR-2021 / 30-MAR-2022	#1) 11 months 23 days
#2) 01-JUL-2022 / 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.
PV202300084709

25b. NAME AND ADDRESS OF REPORTER
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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old female patient received bosutinib (BOSULIF), first regimen from 08Apr2021 to 30Mar2022 at 300 mg daily, second regimen from 31Mar2022 to 30Jun2022 at 200 mg alternate day, oral and third regimen from 31Mar2022 to 30Jun2022 at 300 mg alternate day, oral; dasatinib (DASATINIB), since 01Jul2022 (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "LMC" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: HIATUS HERNIA (non-serious) with onset 2022, outcome "recovering", described as "HIATAL HERNIA"; PERICARDIAL EFFUSION (non-serious) with onset Feb2023, outcome "not recovered". The action taken for dasatinib was dosage permanently withdrawn.

The reporter considered "hiatal hernia" and "pericardial effusion" not related to bosutinib.

Additional information: The event hiatal hernia was rated Grade 2; Action taken for bosutinib was not applicable and dasatinib was no modification; The investigator considered that the event was unrelated to any concomitant medication. The event pericardial effusion was rated Grade 2; Action taken for bosutinib was not applicable and dasatinib was withdrawal; The investigator considered that the event was related to dasatinib.

Follow-up (07Sep2023): This is a follow-up report received from the CRO.
Updated information included: Investigator Initial Aware Date updated, patient details updated (weight), suspect drug Bosulif details updated (start dates, new dosage regimen).

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

Case Comment: Both reported hiatal hernia and pericardial effusion are deemed unrelated to the study drug, bosutinib. Of note, pericardial effusion occurred more than 7 months after the last dose of 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, alternate day; Oral	Unknown	31-MAR-2022 / 30-JUN-2022; 3 months
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, alternate day; Oral	Unknown	31-MAR-2022 / 30-JUN-2022; 3 months

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		JUL	2022

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
Lower limb motor-sensory axonal neuropathy [Axonal neuropathy]
Renal artery stenosis [Renal artery stenosis]

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, 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) Unknown / 20-OCT-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 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.
PV202300084719

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

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

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: PV202300084719

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

for protocol B1871047.

A 77-year-old male patient received bosutinib (BOSULIF), till 20Oct2022 at 300 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: AXONAL NEUROPATHY (medically significant) with onset Jul2022, outcome "not recovered", described as "Lower limb motor-sensory axonal neuropathy"; RENAL ARTERY STENOSIS (non-serious) with onset 01Sep2022, outcome "not recovered". The patient underwent the following laboratory tests and procedures: Computerised tomogram: (01Sep2022) Stenosis of the renal artery more than 75%; Electromyogram: (Jul2022) Lower limb motor-sensory axonal neuropathy. The action taken for bosutinib was dosage permanently withdrawn on 20Oct2022.

The reporter considered 'lower limb motor-sensory axonal neuropathy' related to bosutinib. The reporter considered 'renal artery stenosis' not related to bosutinib.
Reporter's comment: in the continuity of a polymorphic symptomatology, realization multiple examinations including an electromyogram of Jul2022 axonal sensory-motor neuropathy of the 2 lower limbs, qualified as severe. In this context, and in the absence of diabetes, monoclonal peak, proteinuria it is possible that bosutinib be responsible.

Follow-up (17Jul2023): This is a non-interventional study report (Post Authorization Safety Study) received from investigator from CRO for protocol B1871047.
Updated information includes: updated patient's weight, and event 'Lower limb motor-sensory axonal neuropathy' onset date.

Case Comment: Event Lower limb motor-sensory axonal neuropathy is unlisted in the SRSD of BOSUTINIB and related per Company assessment.

Based on available information, a possible contributory role of the subject drug BOSUTINIB cannot be excluded for the reported event Lower limb motor-sensory axonal neuropathy. Event Renal artery stenosis is most likely related to intercurrent or underlying conditions and unrelated to subject drug BOSUTINIB.

The impact of this report on the benefit/risk profile of the Pfizer product is evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators, as appropriate.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-SEP-2022	Computerised tomogram	Stenosis of the renal artery more than 75%	
2	JUL-2022	Electromyogram	Lower limb motor-sensory axonal neuropathy	

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	Male	114.00 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)

Right 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) 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) DASATINIB (DASATINIB)
(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	#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) 23-DEC-2018 / Unknown	#1) Unknown
#2) 04-SEP-2020 / 05-NOV-2020	#2) 2 months 2 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.
PV202300084724

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), first regimen since 23Dec2018 at 200 mg, second regimen since 30Dec2018 at 300 mg, third regimen since 30Jun2019 at 400 mg, fourth regimen since 27Feb2020 at 300 mg and fifth regimen from 11Jul2020 to 03Sep2020 at 200 mg 1x/day (200 mg, 1x/day (intolerance)); dasatinib (DASATINIB), from 04Sep2020 (Batch/Lot number: unknown) to 05Nov2020. The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: PLEURAL EFFUSION (non-serious) with onset 05Nov2020, outcome "recovered" (Nov2020), described as "Right pleural effusion". The action taken for dasatinib was dosage permanently withdrawn on 05Nov2020.
The reporter considered "right pleural effusion" not related to bosutinib.

Additional information: the event "Right pleural effusion" was rated grade 2. According to the investigator, the event Right pleural effusion was unrelated to study drug bosutinib but related to dasatinib. Dasatinib was withdrawn (not clarified if temporarily or permamently, or delayed administration). Resumption of Bosulif on 12Nov2020. Bosulif was already discontinued when the event occurred.

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

Amendment: This follow-up report is being submitted to amend previous information: Patient gender updated to male and patient age added.

Follow-up (07Sep2023): This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician) for protocol B1871047.
Updated information: suspect drug data (dosage regimen and action taken) and clinical course.
Follow-up attempts are completed. No further information is expected.

Follow-up (07Sep2023): This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician) for protocol B1871047.

Updated information: Study drug frequency (fifth dosage regimen) and onset date of the event specified. The dechallenge date of dasatinib was added.

Case Comment: Considering the reported Right pleural effusion occurred around 2 months after the last dose of bosutinib, the Company is in agreement with the reporting investigator, considering the event unrelated to the suspect.

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; Unknown	Unknown	30-DEC-2018 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg; Unknown	Unknown	30-JUN-2019 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	300 mg; Unknown	Unknown	27-FEB-2020 / Unknown; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #5	200 mg, 1x/day (intolerance); Unknown	Unknown	11-JUL-2020 / 03-SEP-2020; 1 month 24 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	Male	78.80 kg	01	SEP	2022

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

RIGHT KIDNEY BENIGN CORTICAL CYST [Renal cyst]
SIGMOID COLON DIVERTICULA [Diverticulum intestinal]

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) 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.
PV202300084766

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), at 300 mg daily. The patient's relevant medical history included: "LMC" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: RENAL CYST (non-serious) with onset 01Sep2022, outcome "not recovered", described as "RIGHT KIDNEY BENIGN CORTICAL CYST"; DIVERTICULUM INTESTINAL (non-serious) with onset 01Sep2022, outcome "not recovered", described as "SIGMOID COLON DIVERTICULA". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.

The reporter considered "right kidney benign cortical cyst" and "sigmoid colon diverticula" not related to bosutinib.

Additional information: The events were assessed as non serious, grade 1. The events were reported as unrelated to the study drug and unrelated to concomitant drugs.

Case Comment: In agreement with the reporter, the Company considers that there is not a reasonable possibility that the study drug bosutinib may have caused the reported events RIGHT KIDNEY BENIGN CORTICAL CYST"; DIVERTICULUM INTESTINAL in this Non-interventional study. The events represents intercurrent medical condition.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	01-SEP-2022	Ultrasound abdomen	Renal cyst and Diverticulum intestinal	

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		75 Years	Female	52.10 kg	17	JAN	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 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
(Continued on Additional Information Page)

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) 06-JAN-2020 / 16-JAN-2020

19. THERAPY DURATION
#1) 11 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	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.
PV202300084778

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

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

DATE OF THIS REPORT
28-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), first regimen from 06Jan2020 to 16Jan2020 at 300 mg 1x/day and second regimen since 17Jan2020 (ongoing) at 200 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 17Jan2020, outcome "recovered" (2020), described as "Diarrhea". The action taken for bosutinib was dosage not changed.

Additional information: Diarrhea was assessed as non serious, grade 1. The event was reported as related to the study drug and unrelated to concomitant drugs. There was no dose change of bosutinib dose in response to diarrhea grade 1.

The reporter considered "diarrhea" related to bosutinib.

Follow-up (07Sep2023): This is a non-interventional study report received from the investigational site via the CRO and clinical team. Updated information: Suspect product dosage regimen and clinical course details.

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

Case Comment: Based on the known drug safety profile, a causal association between bosutinib and the reported event "diarrhea" cannot be excluded.

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	17-JAN-2020 / Ongoing; Unknown

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	Male	79.00 kg	03	NOV	2020

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

Prostatic hypertrophy [Benign prostatic hyperplasia]
Hepatic steatosis [Hepatic steatosis]

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) 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.
PV202300085545

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

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

DATE OF THIS REPORT
28-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 76-year-old male patient received bosutinib (BOSULIF), (ongoing) 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: HEPATIC STEATOSIS (non-serious) with onset 03Nov2020, outcome "not recovered"; BENIGN PROSTATIC HYPERPLASIA (non-serious) with onset 03Nov2020, outcome "not recovered", described as "Prostatic hypertrophy". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.

The reporter considered "prostatic hypertrophy" and "hepatic steatosis" not related to bosutinib.
Additional information: The events were disclosed on abdomen ultrasound performed on 03Nov2020. Events were rated grade 1.

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

Case Comment: In agreement with the reporter, the Company considers that there is not a reasonable possibility that the study drug bosutinib may have caused the reported events hepatic steatosis and benign prostatic hyperplasia in this Non-interventional study.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	03-NOV-2020	Ultrasound abdomen	Hepatic steatosis and prostatic hypertrophy	

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	Male	76.00 kg	10	OCT	2022

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

Psychological state worsened [Mental 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) 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) chronic myeloid leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 01-OCT-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 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.
PV202300088166

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

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

DATE OF THIS REPORT
28-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 76-year-old male patient received bosutinib (BOSULIF), since 01Oct2019 (ongoing) at 300 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: MENTAL DISORDER (non-serious) with onset 10Oct2022, outcome "not recovered", described as "Psychological state worsened". The action taken for bosutinib was dosage not changed.
Additional information: The event mental disorder was rated grade 1 and reported as non-serious.

The reporter considered "psychological state worsened" not related to bosutinib.

Amendment: This follow-up report is being submitted to amend previous information: update patient's gender to male.

Case Comment: Based on very limited available information and action taken for the event, the company concurs with the reporter that "psychological state worsened" was not related to bosutinib. Event is more likely an 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		76 Years	Male	76.00 kg	04	APR	2022

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

Ferritin at lower limit [Serum ferritin decreased]
prostatism [Prostatism]

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 Physician and an 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) 01-OCT-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 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.
PV202300088188

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

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

DATE OF THIS REPORT
28-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 76-year-old male patient received bosutinib (BOSULIF), since 01Oct2019 (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: SERUM FERRITIN DECREASED (non-serious) with onset 04Apr2022, outcome "not recovered", described as "Ferritin at lower limit"; PROSTATISM (non-serious) with onset 10Oct2022, outcome "not recovered".
Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.
Additional information: The events Ferritin at lower limit and prostatism were rated grade 2.
The reporter considered "ferritinemia" and "prostatism" not related to bosutinib or to any concomitant drug.
Follow-up attempts are completed. No further information is expected.

Follow-up (06Dec2023): This is a non-interventional study followreport from the investigational site via the CRO. Updated information includes: the event term "Ferritinemia" was changed to "Ferritin at lower limit", (rated grade 2 from 04Apr2022 and not recovered, unrelated to bosutinib).

Case Comment: Based on very limited available information and action taken, the company concurs with the reporter that reported "Ferritin at lower limit" and "prostatism" were not related to bosutinib but more likely associated with intercurrent or concurrent medical conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	04-APR-2022	Serum ferritin	Ferritinemia	

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	90.00 kg			2020

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

smell and taste disorder [Parosmia]
smell and taste disorder [Taste disorder]
walking difficulty [Gait disturbance]

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

(Continued on Additional Information Page)

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

15. DAILY DOSE(S)
#1) 400 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) 27-NOV-2017 / 27-JAN-2020

19. THERAPY DURATION
#1) 2 years 2 months 1 day

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.
PV202300092644

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300092644

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

for protocol B1871047.

A 73-year-old male patient received bosutinib (BOSULIF), first regimen from 27Nov2017 to 27Jan2020 at 400 mg daily and second regimen since 28Jan2020 (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: PAROSMIA (non-serious), TASTE DISORDER (non-serious) all with onset 2020, outcome "recovered" (2020) and all described as "smell and taste disorder"; GAIT DISTURBANCE (non-serious) with onset 29Sep2020, outcome "recovered" (2020), described as "walking difficulty". The action taken for bosutinib was dosage not changed.

The reporter considered "smell and taste disorder" and "walking difficulty" not related to bosutinib.

Additional information: All the events were rated grade 1. The investigator considered that the events were unrelated to bosutinib or to any concomitant drug.

Case Comment: The company concurs with the reporter that "smell and taste disorder", "walking difficulty" are more likely intercurrent medical conditions and not 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	500 mg, daily; Unknown	Unknown	28-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		54 Years	Male	87.00 kg		JAN	2022

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

dry and irritated eyes [Dry eye]
dry and irritated eyes [Eye irritation]

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) NILOTINIB (NILOTINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 17-OCT-2019 / 23-OCT-2019	#1) 7 days
#2) 27-OCT-2021 / Ongoing	#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.
PV202300092896

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300092896

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 54-year-old male patient received bosutinib (BOSULIF), first regimen from 17Oct2019 to 23Oct2019 at 200 mg daily, second regimen from 24Oct2019 to May2020 at 300 mg daily, third regimen from May2020 to 12Apr2021 at 200 mg daily and fourth regimen from 13Apr2021 to 12Oct2021 at 100 mg daily; nilotinib (NILOTINIB), since 27Oct2021 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient took concomitant medications.
The following information was reported: DRY EYE (non-serious), EYE IRRITATION (non-serious) all with onset Jan2022, outcome "recovered" (25Jan2022) and all described as "dry and irritated eyes". The action taken for nilotinib was dosage not changed.

Additional information: The event was rated Grade 1.

According to the investigator, the event was unrelated to the study drug BOSULIF but related to concomitant drug nilotinib.

Follow-up (31Jul2023): This is a follow-up report from the investigator via CRO. New information received included: removal of previously reported start/stop date and dosage of bosutinib.

Follow-up (02Oct2023): This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information included bosutinib dosages.

Case Comment: Based on the available information and known safety profile, in agreement with the reporting physician, there is not a reasonable possibility that reported "dry and irritated eyes" is related to bosutinib. Event(s) is most likely due to an intercurrent medical condition. Concomitant nilotinib might provide an alternative explanation to the event(s).

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	24-OCT-2019 / MAY-2020; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	MAY-2020 / 12-APR-2021; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	100 mg, daily; Unknown	Unknown	13-APR-2021 / 12-OCT-2021; 6 months

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		53 Years	Female	Unk	09	MAR	2020

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

atheromatous overload AT THE CAROTID LEVEL [Carotid 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) 500 mg, daily

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

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

18. THERAPY DATES(from/to)
#1) 19-MAR-2019 / 27-FEB-2020

19. THERAPY DURATION
#1) 11 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)
#1) ICLUSIG (PONATINIB HYDROCHLORIDE) ; 03-MAR-2020 / 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.
PV202300096932

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

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

DATE OF THIS REPORT
28-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 female patient received bosutinib (BOSULIF), from 19Mar2019 to 27Feb2020 at 500 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: ICLUSIG oral taken for chronic myeloid leukaemia, start date: 03Mar2020 (ongoing).
The following information was reported: CAROTID ARTERIOSCLEROSIS (non-serious) with onset 09Mar2020, outcome "not recovered", described as "atheromatous overload AT THE CAROTID LEVEL". Relevant laboratory tests and procedures are available in the appropriate section.

The reporter considered "atheromatous overload at the carotid level" not related to bosutinib.

Additional information: Moderate to minimal atheroma overload at the carotid level (grade 1, not significant: no action), doppler done in prevention.

Follow-up attempts are not needed. No further information is expected.

Case Comment: Based on the available information, the Company considers the reported event atheromatous overload at the carotid level is unrelated to suspect drug bosutinib but more likely an inter-current medical condition.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Ultrasound Doppler doppler done in prevention	Unknown result	

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	Male	83.00 kg	31	AUG	2020

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

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 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.
PV202300097660

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), (ongoing). The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: URINARY TRACT INFECTION (non-serious) with onset 31Aug2020, outcome "recovered" (05Sep2020), described as "Urinary infection". 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 urinary tract infection.

The reporter considered "urinary infection" not related to bosutinib.

Additional information: The event Urinary infection was rated grade 2. Urine examination pre surgical intervention for prostate; positive therefore treatment Bactrim started from 31Aug2020 to 05Sep2020. The investigator considered that the event was unrelated to Bosulif or to any concomitant drug.

Case Comment: Based on the available information and known safety profile of suspect product, in agreement with reporting physician, the Company considers that there is not a reasonable possibility that event urinary infection was related to bosutinib. Event is most likely an intercurrent medical condition in this 77-yr old man with prostatic problems.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Urine analysis Positive	Positive	

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		75 Years	Male	96.00 kg	15	NOV	2021

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

Edematous syndrome [Oedema]
Acute renal insufficiency [Acute kidney injury]

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 (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) 20-NOV-2019 / 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.
PV202300098634

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 75-year-old male patient received bosutinib (BOSULIF), since 20Nov2019 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: OEDEMA (hospitalization) with onset 15Nov2021, outcome "recovered" (14Dec2021), described as "Edematous syndrome"; ACUTE KIDNEY INJURY (hospitalization) with onset 01Dec2021, outcome "recovered" (14Dec2021), described as "Acute renal insufficiency". The patient was hospitalized for oedema, acute kidney injury (start date: 01Dec2021, discharge date: 14Dec2021, hospitalization duration: 14 day(s)). Comment: flare up of acute renal failure and edematous syndrome, rated grade 3, related to known cardiac insufficiency/ heart failure. Treatment: Lasilix. Initial urgent consultation on 30Nov2021 which precedes hospitalization the next day on 01Dec2021. Hospital release on 14Dec2021. Bosutinib suspension from 01Dec2021 to 21Dec2021. The action taken for bosutinib was temporarily withdrawn.

The reporter considered "edematous syndrome" and "acute renal insufficiency" not related to bosutinib or concomitants medication.

Follow-up (03Jul2023): This is a follow-up non-interventional study report received from a contactable reporter (Physician) for protocol B1871047. Updated information: bosutinib details, onset date of the event edematous syndrome and comment.

Case Comment: Based on the temporal relationship and known AE profile of bosutinib, the reasonable possibility that bosutinib may have contributed to reported "edematous syndrome" and "acute renal insufficiency" cannot be completely ruled out. "known cardiac insufficiency" may have played an important role towards reported events.
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		34 Years	Male	122.00 kg	01	OCT	2019

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

GYNECOLOGICAL INFECTION [Genital infection female]
MUSCLE PAIN [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) 300 mg, daily

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

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

18. THERAPY DATES(from/to)
#1) 11-DEC-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) ASCIMINIB (ASCIMINIB) ; 07-OCT-2020 / 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.
PV202300102409

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

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

DATE OF THIS REPORT
28-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 34-year-old male patient received bosutinib (BOSULIF), since 11Dec2018 (ongoing) at 300 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: ASCIMINIB oral taken for chronic myeloid leukaemia, start date: 07Oct2020 (ongoing).
The following information was reported: GENITAL INFECTION FEMALE (non-serious) with onset 01Oct2019, outcome "recovered" (15Oct2019), described as "GYNECOLOGICAL INFECTION"; MYALGIA (non-serious) with onset Oct2020, outcome "recovered" (16Mar2021), described as "MUSCLE PAIN". The action taken for bosutinib was dosage not changed.

The reporter considered "gynecological infection" and "muscle pain" not related to bosutinib and to concomitant drug.

Additional information: The event gynecological infection was rated non-serious with grade 2 and the event muscle pain was rated non-serious with grade 1. The action taken in response to the event gynecological infection was reported as dose not changed for the study drug bosutinib. The action taken in response to the event muscle pain was reported as not applicable for the study drug bosutinib and dose not changed for the concomitant drug asciminib.

Case Comment: Both reported "gynecological infection" and "muscle pain" are considered unrelated to the suspect, bosutinib. Events recovered without dosage change 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		70 Years	Female	63.00 kg	17	JAN	2018

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]
Right lumbar scoliosis [Scoliosis]

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) chronic myeloid leukaemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 28-NOV-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 to Ongoing	Relevant Med History	Chronic myeloid leukaemia (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.
PV202300102987

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

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

DATE OF THIS REPORT
28-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 patient received bosutinib (BOSULIF), since 28Nov2017 (ongoing) at 500 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukaemia (CML)" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: HEPATIC CYTOLYSIS (non-serious) with onset 17Jan2018, outcome "recovered" (28Feb2018); SCOLIOSIS (non-serious) with onset 11Dec2018, outcome "not recovered", described as "Right lumbar scoliosis". The action taken for bosutinib was dosage not changed.
The reporter considered "hepatic cytolysis" related to bosutinib. The reporter considered "right lumbar scoliosis" not related to bosutinib.

Additional information: Both events were rated grade 1.

Follow-up (20Jul2023): This is a non-interventional study follow-up report from the investigational site. Updated information: onset date of event "hepatic cytolysis", start date of bosutinib.

Case Comment: Events 'hepatic cytolysis' and 'right lumbar scoliosis' represent intercurrent medical conditions and unrelated to bosutinib.

The impact of this report on the benefit/risk profile of the Pfizer product is evaluated as part of Pfizer procedures for safety evaluation, including the review and analysis of aggregate data for adverse events. Any safety concern identified as part of this review, as well as any appropriate action in response, will be promptly notified to Regulatory Authorities, Ethics Committees and Investigators, as appropriate.

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	63.00 kg	03	SEP	2019

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

Hearing decreased [Hypoacusis]

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 Physician for protocol B1871047.

A 72-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) 500 mg, 1x/day

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

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

18. THERAPY DATES(from/to)
#1) 02-JUL-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
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.
PV202300103038

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

(BOSULIF), since 02Jul2018 (ongoing) at 500 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: HYPOACUSIS (non-serious) with onset 03Sep2019, outcome "not recovered", described as "Hearing decreased". The action taken for bosutinib was dosage not changed.

Additional information: the event 'hearing decreased' was assessed as non-serious and rated grade 1.

According to the investigator, the event Hearing decreased was unrelated to study drug and to concomitant drug.

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

Case Comment: The Company agrees with the assessment of the investigator and reasonably does not attribute the event "hearing decreased" to study drug and concomitant drug based on the information currently available and the pathophysiology of the event. Event is likely an inter-current disease in this elderly female patient.

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		71 Years	Female	63.00 kg	11	DEC	2018

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

Discarthrosis L2 to L5 [Intervertebral disc degeneration]

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) 02-JUL-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
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.
PV202300103045

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

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

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: PV202300103045

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 71-year-old female patient received bosutinib (BOSULIF), since 02Jul2018 (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: INTERVERTEBRAL DISC DEGENERATION (non-serious) with onset 11Dec2018, outcome "not recovered", described as "Discarthrosis L2 to L5". The action taken for bosutinib was dosage not changed.

Additional information: The event was rated grade 1. Event reported as non-serious. The event outcome was not recovered / not resolved. Action taken was: dose not changed. The investigator considered that the event was unrelated to bosutinib or to any concomitant drug.

The reporter considered "discarthrosis l2 to l5" not related to bosutinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the information available, the company concurs with the investigator that event "discarthrosis L2 to L5" is unrelated to bosutinib. The event is most likely an intercurrent condition in this elderly 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		78 Years	Male	83.00 kg	08	MAR	2021

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

Aggravation of chronic renal insufficiency [Chronic kidney disease]

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) 300 mg, daily

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

17. INDICATION(S) FOR USE
#1) chronic myeloid leukemia in chronic pha
(Continued on Additional Information Page)

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

18. THERAPY DATES(from/to)
#1) 03-JUL-2019 / 07-MAR-2021

19. THERAPY DURATION
#1) 1 year 8 months 5 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	Creatinine high (Blood creatinine increased)
Unknown	Relevant Med History	Renal failure (Renal failure)

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.
PV202300115539

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old male patient received bosutinib (BOSULIF), first regimen from 03Jul2019 to 07Mar2021 at 300 mg daily and second regimen since 08Mar2021 (ongoing) at 200 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "high creatinine level" (unspecified if ongoing); "renal failure" (unspecified if ongoing). There were no concomitant medications.
The following information was reported: CHRONIC KIDNEY DISEASE (non-serious) with onset 08Mar2021, outcome "not recovered", described as "Aggravation of chronic renal insufficiency". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage reduced.

The reporter considered "aggravation of chronic renal insufficiency" not related to bosutinib.

Additional information: In total chronic myeloid leukemia in chronic phase under bosutinib reduced to 200 mg/day due to chronic renal failure increasing since the beginning of treatment. In persisting major molecular response after 24 months. Event aggravation of chronic renal failure was reported as non-serious event, grade 1. The event was assessed as not related to the study drug and any concomitant drug.

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

Follow-up (18Jul2023 and 19Jul2023): 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: concomitant drug details (none) and medical history(high creatinine level- renal failure).

Case Comment: Based on the limited information provided and known safety profile of the suspect drug, the Company cannot completely exclude the possible causality between the reported "aggravation of chronic renal insufficiency" and bosutinib administration.
The follow up information does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Investigation	persisting major molecular response	

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 #1	300 mg, daily; Unknown	chronic myeloid leukemia in chronic phase (Chronic myeloid leukaemia)	03-JUL-2019 / 07-MAR-2021; 1 year 8 months 5 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #2	200 mg, daily; Unknown	chronic myeloid leukemia in chronic phase (Chronic myeloid leukaemia)	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		78 Years	Male	83.00 kg		JAN	2021

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

Toxicity related to chemotherapy [Toxicity to various agents]

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) FIRMAGON (DEGARELIX ACETATE)
(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) 300 mg, daily	#1) Unknown
#2) UNK	#2) Unknown

17. INDICATION(S) FOR USE
#1) Unknown
#2) hormone-sensitive prostatic adenocarcinoma (Adenocarcinoma)

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 07-DEC-2020 / 07-MAR-2021	#1) 3 months 1 day
#2) 07-JAN-2021 / 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	Relevant Med History	Adenocarcinoma (Adenocarcinoma) carcinoma of the prostate treated by ABIRATERONE and FIRMAGON since 07Jan2021
Unknown	Relevant Med History	Diabetes mellitus (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.
PV202300115549

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old male patient received bosutinib (BOSULIF), first regimen from 07Dec2020 to 07Mar2021 at 300 mg daily and second regimen since 08Mar2021 (ongoing) at 200 mg daily; degarelix acetate (FIRMAGON), since 07Jan2021 (Batch/Lot number: unknown) for adenocarcinoma; abiraterone (ABIRATERONE), since 07Jan2021 (Batch/Lot number: unknown) for adenocarcinoma; prednisone (CORTANCYL), (Batch/Lot number: unknown) for diabetes mellitus. The patient's relevant medical history included: "ADENOCARCINOMA PROSTATITIS" (unspecified if ongoing), notes: carcinoma of the prostate treated by ABIRATERONE and FIRMAGON since 07Jan2021; "Diabetes mellitus" (unspecified if ongoing). The patient's concomitant medications were not reported. The following information was reported: TOXICITY TO VARIOUS AGENTS (non-serious) with onset Jan2021, outcome "recovering", described as "Toxicity related to chemotherapy". The action taken for bosutinib, degarelix acetate and abiraterone was dosage not changed; for prednisone was unknown.

Additional information: Tolerance to treatment was good, marked by asthenia especially in the afternoon, grade I constipation and some nausea. He did not provide his blood pressure reading but it seemed that it was on the rise. Diabetes was unbalanced by cortancyl with the need to adapt insulin doses. Fluctuating bilateral lower limb edema of non-pitting type, without dyspnea. Absence of bone pain. There persisted significant urinary leakage with 4 nocturnal sunrises. All the events were rated as grade 1 and were further described and reported as "toxicity related to chemotherapy". No seriousness criteria was provided. Treatment given: BOSEVAL. In hospitalization report dated 29Apr2021 it was reported that the patient's sleep was average quality due to the functional urinary signs with repeat nocturnal standing, decrease appetite alters transit, with alterating constipation grade 1 and light diarrheas.

The reporter considered "toxicity related to chemotherapy", not related to bosutinib and related to FIRMAGON and ABIRATERONE.

Follow-up (12Jul2023): 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: Outcome of all the events were updated to recovering.

Follow-up (05Oct2023): This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information includes: all previously reported events were subsumed under new event "toxicity related to chemotherapy" grade 1, action taken with degarelix acetate and abiraterone updated from "Unknown" to "Dose not changed" and clinical course provided.

Case Comment: In concurrence with the Investigator, the reported event, Toxicity to various agents, is deemed related to chemotherapeutic agents, degarelix acetate (FIRMAGON) and abiraterone (ABIRATERONE), 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	08-MAR-2021 / Ongoing; Unknown
#3) ABIRATERONE (ABIRATERONE) ; Regimen #1	UNK; Unknown	hormone-sensitive prostatic adenocarcinoma (Adenocarcinoma)	07-JAN-2021 / Unknown; Unknown
#4) CORTANCYL (PREDNISONE) ; Regimen #1	UNK; Unknown	Diabetes (Diabetes mellitus)	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		75 Years	Male	96.00 kg	01	DEC	2021

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

Thoracic pain [Chest 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 a contactable Physician for protocol B1871047.

A 75-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) 300 mg

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) 20-NOV-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 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.
PV202300117157

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
28-FEB-2024

25a. REPORT TYPE
- ☒ INITIAL
- ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

20Nov2019 (ongoing) at 300 mg taken for chronic myeloid leukemia. The patient's relevant medical history included: 'Chronic myeloid leukemia' (ongoing). The patient's concomitant medications were not reported.
The following information was reported: CHEST PAIN (hospitalization) with onset 01Dec2021, outcome 'recovered' (12Jan2022), described as 'Thoracic pain'. The action taken for bosutinib was dosage not changed.

Additional information: the oppression occurred during the previous hospitalization for acute renal insufficiency. Hospitalization for scheduled workup from 10 to 12Jan2022: workup without evolution compared to previous cardiac situation known. No new thoracic pain.

The reporter considered 'thoracic pain' not related to bosutinib.

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

Case Comment: The company concurs with the reporter that 'thoracic pain', occurred more than 2 years after starting bosutinib, is unrelated to bosutinib. Subject's underlying 'Chronic myeloid leukemia' may alternatively explain 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	100.00 kg		Unk	

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

placement of total left knee prosthesis due to arthrosis of the knee [Osteoarthritis]

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, daily

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

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

18. THERAPY DATES(from/to)
#1) 08-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)

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 leukaemia (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.
PV202300117206

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old male patient received bosutinib (BOSULIF), since 08Jul2019 (ongoing) at 500 mg daily. The patient's relevant medical history included: "Chronic myeloid leukaemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: OSTEOARTHRITIS (non-serious), outcome "recovered" (Sep2021), described as "placement of total left knee prosthesis due to arthrosis of the knee". The action taken for bosutinib was dosage not changed. Therapeutic measures were taken as a result of osteoarthritis.

The reporter considered "placement of total left knee prosthesis due to arthrosis of the knee" not related to bosutinib.

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: event term and coding were updated.

Follow-up (31Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from the investigational site for protocol B1871047. Updated information: event onset date.

Case Comment: Based on the available information, the Company considers the reported event "placement of total left knee prosthesis due to arthrosis of the knee" is unrelated to suspect drug bosutinib but more likely due to underlying or an inter-current medical condition.
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		73 Years	Male	100.00 kg		JAN	2022

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

Hematuric episode [Haematuria]
Anguish [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 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) BRILIQUE (TICAGRELOR)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, 1x/day	#1) Unknown
#2)	#2) Unknown

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 08-JUL-2019 / Ongoing	#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 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.
PV202300117253

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 73-year-old male patient received bosutinib (BOSULIF), since 08Jul2019 (ongoing) at 500 mg 1x/day; ticagrelor (BRILIQUE), (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: ANXIETY (non-serious) with onset Jan2022, outcome "recovered" (14Feb2022), described as "ANGUISH"; HAEMATURIA (non-serious) with onset Jan2022, outcome "recovered" (14Feb2022), described as "HEMATURIC EPISODE". The action taken for bosutinib was dosage not changed. The action taken for ticagrelor was temporarily withdrawn.

Additional information: Both events were rated grade 1.

The reporter considered "hematuric episode" not related to the study drug bosulif but related to drug ticagrelor while "anguish" not related to bosutinib and ticagrelor.

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

Case Comment: Based on the information available, the events "hematuric episode" and "anguish" are most likely intercurrent conditions and 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		
		Day	Month	Year				Day	Month	Year
PRIVACY	FRANCE		PRIVACY		61 Years	Male	Unk	09	DEC	2020

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

Hypertriglyceridemia [Hypertriglyceridaemia]

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) LOXEN [NICARDIPINE HYDROCHLORIDE] (NICARDIPINE **(Continued on Additional Information Page)**

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) UNK, 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) 30-JAN-2019 / Unknown	#1) Unknown
#2) Ongoing	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

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	Acute myeloid leukemia (Acute 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.
PV202300117254

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

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 61-year-old male patient received bosutinib (BOSULIF), first regimen since 30Jan2019 at daily (unk, daily) and second regimen since 25Sep2020 (ongoing) at 100 mg daily; nicardipine hydrochloride (LOXEN [NICARDIPINE HYDROCHLORIDE]), (ongoing) (Batch/Lot number: unknown). The patient's relevant medical history included: "Acute myeloid leukemia" (ongoing). The patient's concomitant medications were not reported. The following information was reported: HYPERTRIGLYCERIDAEMIA (non-serious) with onset 09Dec2020, outcome "recovered" (2021), described as "Hypertriglyceridemia". The action taken for bosutinib was 'dose not changed'; for nicardipine hydrochloride was dosage not changed.

Additional information: Hypertriglyceridemia was grade 1. Bosulif dose was decreased to 100 mg x/1 day on 25Sep2020 due to Hypertension arterial before the event hypertriglyceridemia. Causality was assessed as unrelated to study drug, related to concomitant treatment Loxen.

The reporter considered "hypertriglyceridemia" not related to bosutinib.

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

Follow-up (23Aug2023): This is a follow-up non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.
Updated information included: action taken, dosage regimen of bosutinib updated, event grade and clinical event course.

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

Follow-up (04Oct2023). This follow-up is received from the clinical team:
Updated information includes: Action taken with study drug in response to event Hypertriglyceridemia was updated.

Case Comment: The company concurs with the reporter that "hypertriglyceridemia" is not related to bosutinib but related to concomitant treatment Loxen. 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	100 mg, daily; Unknown	Unknown	25-SEP-2020 / Ongoing; Unknown
#2) LOXEN [NICARDIPINE HYDROCHLORIDE] (NICARDIPINE HYDROCHLORIDE) ; Regimen #1	UNK; Unknown	Unknown	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		84 Years	Female	60.00 kg		OCT	2018

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

E. COLI URINARY INFECTION [Urinary tract infection bacterial]

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) 100 mg, 1x/day

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

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

18. THERAPY DATES(from/to)
#1) 24-JUL-2016 / 30-JUL-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.
PV202300119456

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

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

DATE OF THIS REPORT
28-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

An 84-year-old female patient received bosutinib (BOSULIF), first regimen from 24Jul2016 to 30Jul2016 at 100 mg 1x/day and second regimen since 31Jul2016 (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: URINARY TRACT INFECTION BACTERIAL (non-serious) with onset Oct2018, outcome "recovering", described as "E. COLI URINARY INFECTION". The action taken for bosutinib was dosage not changed.

Additional information: The event urinary tract infection bacterial was rated grade 2. The event was reported as non-serious. The investigator considered that the event was unrelated to BOSULIF or to any concomitant drug.

The reporter considered "E. coli urinary infection" not related to bosutinib.

Follow-up (02Aug2023): 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: dosage regimen of suspect product updated, patient details updated.

Follow-up (04Oct2023): 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: the patient had no relevant medical history.

Case Comment: Based on the information currently available, the reported "E. coli urinary infection" considered unrelated to 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	200 mg, 1x/day; Unknown	Unknown	31-JUL-2016 / 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		67 Years	Male	115.00 kg		OCT	2021

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

Hypertension aggravation [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

(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) 02-MAY-2019 / 08-MAY-2019

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	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.
PV202300119467

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300119467

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old male patient received bosutinib (BOSULIF), first regimen from 02May2019 to 08May2019 at 100 mg 1x/day, second regimen from 09May2019 to 22May2019 at 200 mg 1x/day and third regimen since 23May2019 (ongoing) at 300 mg 1x/day. The patient had no relevant medical history. The patient's concomitant medications were not reported.
The following information was reported: HYPERTENSION (non-serious) with onset Oct2021, outcome "recovered" (12May2022), described as "Hypertension aggravation". The action taken for bosutinib was dosage not changed.

The investigator considered that the event was related to bosutinib.

Additional information: The event Hypertension aggravated was rated grade 2. Event reported as non-serious.

Follow-up (31Jul2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from the investigator via the CRO for protocol B1871047.
Updated information: Medical history updated as none, dose regimen of bosutinib updated.

Case Comment: Based on the known drug safety profile, a causal association between bosutinib and the event hypertension cannot be 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	200 mg, 1x/day; Unknown	Unknown	09-MAY-2019 / 22-MAY-2019; 14 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, 1x/day; Unknown	Unknown	23-MAY-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		63 Years	Male	117.00 kg		FEB	2019

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

Asthmatic bronchitis [Asthma]

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) 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, 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) 23-NOV-2017 / 01-MAY-2018	#1) 5 months 9 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.
PV202300125169

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300125169

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 63-year-old male patient received bosutinib (BOSULIF), first regimen from 23Nov2017 to 01May2018 at 100 mg 1x/day and second regimen from 02May2018 to 29May2018 at 200 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: ASTHMA (non-serious) with onset Feb2019, outcome "recovered" (2019), described as "Asthmatic bronchitis".

The reporter considered "asthmatic bronchitis" not related to bosutinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: Event asthmatic bronchitis represents 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, 1x/day; Unknown	Unknown	02-MAY-2018 / 29-MAY-2018; 28 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		54 Years	Female	60.70 kg		JAN	2022

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

Cruralgia [Sciatica]
Hernia [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 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	#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) 05-JAN-2020 / 11-JAN-2020	#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) ; AUG-2020 / 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.
PV202300125178

25b. NAME AND ADDRESS OF REPORTER
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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 54-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), first regimen from 05Jan2020 to 11Jan2020 at 200 mg, second regimen from 12Jan2020 to 05Apr2020 at 300 mg, third regimen from 30Apr2020 to Jun2020 at 200 mg daily and fourth regimen from Jun2020 to 26Aug2020 at 300 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: Aug2020 (ongoing). The following information was reported: SCIATICA (non-serious) with onset Jan2022, outcome "not recovered", described as "Cruralgia"; HERNIA (non-serious) with onset Jan2022, outcome "not recovered".

The reporter considered "cruralgia" and "hernia" not related to bosutinib.

Additional information: The action taken for nilotinib was dose not changed. Cruralgia rated as grade 2 and hernia as grade 1. Event not related to study drug bosutinib or concomitant drug.

Follow-up (07Sep2023, 07Sep2023): These are two follow-up reports from clinical team and from the investigtaor via CRO. New information received included: New reporter, Dosage regimen information of BOSULIF.

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

Case Comment: The reported events sciatica and hernia are intercurrent medical conditions 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	300 mg; Unknown	Unknown	12-JAN-2020 / 05-APR-2020; 2 months 25 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	30-APR-2020 / JUN-2020; Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	300 mg, daily; Unknown	Unknown	JUN-2020 / 26-AUG-2020; Unknown

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		60 Years	Male	104.00 kg	02	JUL	2020

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

Abdominal and thighs folliculitis [Folliculitis]

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	#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) 22-APR-2018 / 01-MAY-2018	#1) 10 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.
PV202300125269

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

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

DATE OF THIS REPORT
28-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 60-year-old male patient received bosutinib (BOSULIF), first regimen from 22Apr2018 to 01May2018 at 100 mg, second regimen from 02May2018 to 11May2018 at 200 mg daily, third regimen from 12May2018 to 31Mar2020 at 300 mg daily, fourth regimen from 01Apr2020 to 06Apr2020 at 200 mg daily and fifth regimen since 07Apr2020 (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: FOLLICULITIS (non-serious) with onset 02Jul2020, outcome "recovered" (2020), described as "Abdominal and thighs folliculitis". The action taken for bosutinib was dosage not changed.

Additional information: The event was rated non serious with grade 1.

The reporter considered "abdominal and thighs folliculitis" not related to bosutinib.

Follow-up (07Sep2023): 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: suspect drug information (new dosage regimens of Bosulif).

Case Comment: In concurrence with the investigator, based on the available information, the event "abdominal and thighs folliculitis" was most likely intercurrent condition and unrelated to the 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, daily; Unknown	Unknown	02-MAY-2018 / 11-MAY-2018; 10 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, daily; Unknown	Unknown	12-MAY-2018 / 31-MAR-2020; 1 year 10 months 20 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	200 mg, daily; Unknown	Unknown	01-APR-2020 / 06-APR-2020; 6 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #5	300 mg, daily; Unknown	Unknown	07-APR-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	76.30 kg		JUN	2022

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

chronic renal failure [Chronic kidney disease]
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
#2) NILOTINIB (NILOTINIB)

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 300 mg, 1x/day	#1) Unknown
#2) UNK	#2) Oral

17. INDICATION(S) FOR USE
#1) Unknown
#2) 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-OCT-2020 / 16-JAN-2021	#1) 2 months 24 days
#2) 04-FEB-2021 / Ongoing	#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.
PV202300125847

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old male patient received bosutinib (BOSULIF), from 24Oct2020 to 16Jan2021 at 300 mg 1x/day; nilotinib (NILOTINIB), since 04Feb2021 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: CHRONIC KIDNEY DISEASE (non-serious) with onset Jun2022, outcome "not recovered", described as "chronic renal failure"; DIARRHOEA (non-serious) with onset 05Oct2022, outcome "recovered" (10Oct2022), described as "diarrhea". The action taken for nilotinib was dosage not changed.

The reporter considered "chronic renal failure" and "diarrhea" not related to bosutinib.

Additional information: Events were rated grade 3, non-serious, considered as unrelated to the study drug but related to concomitant drug NILOTINIB.

Case Comment: Based on the limited available information, there is not a reasonable possibility to consider reported events chronic renal failure and diarrhoea as related to bosutinib, in agreement with reporting physician's opinion. Events were most likely intercurrent medical conditions in this 78-yr old man. Concomitant treatment with nilotinib might provide an 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		71 Years	Male	72.00 kg		SEP	2019

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

Pneumopathy [Lung disorder]
Bronchitis [Bronchitis]

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, 1x/day

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

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

18. THERAPY DATES(from/to)
#1) 10-JAN-2019 / 11-SEP-2019

19. THERAPY DURATION
#1) 8 months 2 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	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.
PV202300125874

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

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

DATE OF THIS REPORT
28-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), from 10Jan2019 to 11Sep2019 at 500 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: LUNG DISORDER (hospitalization) with onset Sep2019, outcome "recovered" (11Oct2019), described as "Pneumopathy"; BRONCHITIS (non-serious) with onset 18Sep2019, outcome "recovered" (23Sep2019).

Additional information: Bronchitis was reported as grade 2 and non-serious, while pneumopathy was reported as grade 3 and serious.

The reporter considered "pneumopathy" and "bronchitis" not related to bosutinib and not related to concomitant drugs.

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

Case Comment: Based on limited available information, relationship between "pneumopathy" and the other reported event "bronchitis" is not provided, the company concurs with the reporter that "pneumopathy" was not related to bosutinib, event was more likely an intercurrent medical condition. Event will be reassessed when additional information is available. Based on the temporal relationship and known AE profile of bosutinib, the reasonable possibility of an association between "bronchitis" 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		36 Years	Female	92.00 kg		JUL	2017

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

Mixed dyslipidaemia [Dyslipidaemia]
Blood glucose imbalance [Blood glucose abnormal]

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) NILOTINIB (NILOTINIB)
(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
#2) UNK	#2) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 18-APR-2016 / 01-MAY-2016	#1) 14 days
#2) 01-JUL-2017 / Ongoing	#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 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.
PV202300125940

25b. NAME AND ADDRESS OF REPORTER
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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 36-year-old female patient received bosutinib (BOSULIF), first regimen from 18Apr2016 to 01May2016 at 100 mg daily, second regimen from 02May2016 to 15May2016 at 200 mg daily, third regimen from 16May2016 to 20Apr2017 at 300 mg daily and fourth regimen from 21Apr2017 to 30Jun2017 at 400 mg daily; nilotinib (NILOTINIB), since 01Jul2017 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: BLOOD GLUCOSE ABNORMAL (non-serious) with onset Jul2017, outcome "not recovered", described as "Blood glucose imbalance"; DYSLIPIDAEMIA (non-serious) with onset 26Oct2017, outcome "not recovered", described as "Mixed dyslipidaemia". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for nilotinib was dosage not changed.

Additional information: both events were assessed as non-serious and rated grade 2. Both events were assessed as related to concomitant nilotinib.

The reporter considered "mixed dyslipidaemia" and "blood glucose imbalance" not related to bosutinib.

Follow-up (07Sep2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from contactable reporters (Physician and Other HCP) for protocol B1871047.
Updated information included: medical history of chronic myelogenous leukemia is ongoing, suspect drug details (new dosage regimens of Bosulif).

Case Comment: In concurrence with the investigator, the reported "mixed dyslipidaemia" and "blood glucose imbalance" are unrelated to the study drug, bosutinib, however are related to concomitant nilotinib. The events are not consistent with the known drug safety profile of bosutinib, however are known to be associated with nilotinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood glucose	imbalance	

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	02-MAY-2016 / 15-MAY-2016; 14 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	300 mg, daily; Unknown	Unknown	16-MAY-2016 / 20-APR-2017; 11 months 5 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	400 mg, daily; Unknown	Unknown	21-APR-2017 / 30-JUN-2017; 2 months 10 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		67 Years	Female	Unk		FEB	2018

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]
Fall (having caused facial bruises) [Fall]
Fall (having caused facial bruises) grade 1 [Contusion]

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) 14-SEP-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.
PV202300127226

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

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

DATE OF THIS REPORT
28-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 67-year-old female patient (unknown if pregnant) received bosutinib (BOSULIF), since 14Sep2017 (ongoing) at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: FALL (non-serious) with onset Feb2018, outcome "recovered" (12Jun2018), described as "Fall (having caused facial bruises)"; CONTUSION (non-serious) with onset Feb2018, outcome "recovered" (12Jun2018), described as "Fall (having caused facial bruises) grade 1"; DIARRHOEA (non-serious) with onset Aug2018, outcome "recovered" (14Sep2018), described as "Diarrhea grade 1". The action taken for bosutinib was dosage not changed.

The reporter considered "diarrhea grade 1" related to bosutinib. The reporter considered "fall (having caused facial bruises)" and "fall (having caused facial bruises) grade 1" not related to bosutinib.
Additional information: The events were reported as non-serious. The investigator considered events were not related to any concomitant drug.

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

Case Comment: The company concurs with the reporter that "diarrhea grade 1" was related to bosutinib considering drug-event temporal relationship and known AE profile of bosutinib, while "fall (having caused facial bruises) grade 1" was not related to bosutinib but more likely intercurrent 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		Unk	Female	Unk		AUG	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
Miscarriage [Abortion spontaneous]

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

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) 21-MAR-2019 / 30-MAR-2020

19. THERAPY DURATION
#1) 1 year 10 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) DASATINIB (DASATINIB) ; 31-MAR-2020 / 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		Date of LMP for pregnancy

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.
PV202300129493

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A female patient (pregnant) was exposed to bosutinib (BOSULIF), via the father of the fetus/baby, administration details for the father: from 21Mar2019 to 30Mar2020 at 500 mg daily. The patient's relevant medical history was not reported. Concomitant medication(s) included: DASATINIB oral taken for chronic myeloid leukaemia, start date: 31Mar2020 (ongoing).
The following information was reported: ABORTION SPONTANEOUS (medically significant) with onset Aug2020, outcome "recovered" (Aug2020), described as "Miscarriage". The pregnancy resulted in spontaneous abortion. The fetal outcome is intrauterine death.

The reporter considered "miscarriage" not related to bosutinib.

Additional information: Subject (the father of the fetus) was 34 years old at the event onset, he had no medical history. Responsibility for the miscarriage not documented in the medical file. Acknowledgment by the investigator: 21Dec2020 acknowledgment, Knowledge by the SC: 25Jul2023. The investigator considered that Miscarriage was unrelated to Bosulif or to any concomitant drug. It was further reported that the pregnancy of the patient's partner started in Jun2020 therefore 3-4 months after the patient has stopped bosutinib.

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

Follow-up (20Sep2023): This is a follow up non-interventional study report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047. Updated information: relationship.

FollFollow-up (28Sep2023): This is a follow up non-interventional study report received from clinical team for protocol B1871047. Updated information includes: details about start period of the pregnancy.

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

Amendment: This follow-up report is being submitted to amend previous information: Patient ID.

Case Comment: Event Miscarriage represents an intercurrent medical condition and unrelated to bosutinib. The underlying disease may also provide an explanation. More information such as complete medical history and concomitant medications are needed for fully medical assessment.

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		33 Years	Male	96.00 kg	30	JAN	2020

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

Hepatic steatosis [Hepatic steatosis]
Hypertriglyceridemia [Hypertriglyceridaemia]

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, 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) 12-NOV-2018 / 26-DEC-2018	#1) 1 month 15 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) DASATINIB (DASATINIB) ; 31-MAR-2020 / 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	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.
PV202300129521

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 33-year-old male patient received bosutinib (BOSULIF), first regimen from 12Nov2018 to 26Dec2018 at 200 mg daily, second regimen from 27Dec2018 to 14Jan2019 at 300 mg daily, third regimen from 15Jan2019 to 20Mar2019 at 400 mg daily and fourth regimen from 21Mar2019 to 30Mar2020 at 500 mg daily. The patient's relevant medical history included: "CML" (ongoing).
Concomitant medication(s) included: DASATINIB oral taken for chronic myeloid leukaemia, start date: 31Mar2020 (ongoing).
The following information was reported: HEPATIC STEATOSIS (non-serious) with onset 30Jan2020, outcome "not recovered"; HYPERTRIGLYCERIDAEMIA (non-serious) with onset 14Apr2020, outcome "recovered" (17Oct2020), described as "Hypertriglyceridemia". Relevant laboratory tests and procedures are available in the appropriate section. The action taken for bosutinib was dosage not changed.
Additional information: Both events were rated grade 1. Action taken on dasatinib in response to event hypertriglyceridemia was dose not changed.

The reporter considered "hepatic steatosis" and "hypertriglyceridemia" not related to bosutinib.

Follow-up (28Sep2023): This is a non-interventional study follow-up report received from the investigational site via the CRO for protocol B1871047.
Updated information includes: medical history (ongoing CML), stop date of 500 mg regimen, and lab (ultrasound).

Case Comment: Available information is very limited, the company concurs with the reporter that "hepatic steatosis" and "hypertriglyceridemia" were not related to bosutinib. Case will be reassessed when additional information is available.
The follow up information does not alter the previous company clinical evaluation.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Ultrasound scan	unknown result	

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	27-DEC-2018 / 14-JAN-2019; 19 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	400 mg, daily; Unknown	Unknown	15-JAN-2019 / 20-MAR-2019; 2 months 6 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #4	500 mg, daily; Unknown	Unknown	21-MAR-2019 / 30-MAR-2020; 1 year 10 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		35 Years	Male	96.00 kg	30	SEP	2021

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
#2) DASATINIB (DASATINIB)

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg	#1) Oral
#2) UNK	#2) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-MAR-2019 / 30-MAR-2020	#1) 1 year 10 days
#2) 31-MAR-2020 / Ongoing	#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
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Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
PV202300129527

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 35-year-old male patient received bosutinib (BOSULIF), from 21Mar2019 to 30Mar2020 at 500 mg, oral; dasatinib (DASATINIB), since 31Mar2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: HEPATIC CYTOLYSIS (non-serious) with onset 30Sep2021, outcome "not recovered". The action taken for dasatinib was dosage not changed.

The reporter considered "hepatic cytolysis" not related to bosutinib, while related to concomitant dasatinib.

Follow-up (28Sep2023): This is a follow-up spontaneous report received from CRO.
Updated information includes: The patient's medical history included ongoing chronic myeloid leukemia.

Case Comment: Based upon the limited set of information, the event hepatic cytolysis, is deemed in agreement with the reporter, as unrelated to bosutinib and related to dasatinib.

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	52.00 kg		APR	2019

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

Essential glossodynia [Glossodynia]

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) 300/200 mg alternately, daily

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

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

18. THERAPY DATES(from/to)
#1) 26-FEB-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
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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26. REMARKS

24b. MFR CONTROL NO.
PV202300129529

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

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

DATE OF THIS REPORT
28-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 69-year-old female patient received bosutinib (BOSULIF), since 26Feb2018 (ongoing) at daily (300/200 mg alternately, 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: GLOSSODYNIA (non-serious) with onset Apr2019, outcome "not recovered", described as "Essential glossodynia". The action taken for bosutinib was dosage not changed.

Additional information: Event essential glossodynia is non-serious, rate grade 2. The patient had essential glossodynia, probably her tongue kept in "memory" the pain that she can have been felt during the lichen episode. Regarding the lichen episode mentioned, there is no pre-existing medical condition or event experienced by the patient during the study, note of the physician during medical consultation: lingual or oral mycosis with several treatments: TRIFLUCAN and FUNGIZONE. Picture taken of the tongue and showed to dermatologist who ruled out the diagnosis of mycosis and stopped antifungal treatment. Treatment with mouthwash with only bicarbonate and mycological sample in 2 weeks if lesions persist.

The reporter considered "essential glossodynia" not related to bosutinib.

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

Follow-up (27Sep2023): This is a follow-up to a non-interventional study for protocol B9991045 received from clinical team.
Updated information included: clinical course.

Case Comment: In concurrence with the investigator, based on the available information, the event "essential glossodynia" was most likely an intercurrent condition and 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			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET		
		Day	Month	Year				Day	Month	Year
PRIVACY	FRANCE		PRIVACY		34 Years	Male	96.00 kg	14	SEP	2020

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

granular lymphocytes [Lymphocyte morphology abnormal]

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 34-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) DASATINIB (DASATINIB)

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
#2) UNK	#2) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-MAR-2019 / 30-MAR-2020	#1) 1 year 10 days
#2) 31-MAR-2020 / Ongoing	#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
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66 Hudson Boulevard East
New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
PV202300129537

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
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

21Mar2019 to 30Mar2020 at 500 mg daily; dasatinib (DASATINIB), since 31Mar2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: LYMPHOCYTE MORPHOLOGY ABNORMAL (non-serious) with onset 14Sep2020, outcome "not recovered", described as "granular lymphocytes". The action taken for dasatinib was dosage not changed, for bosutinib was post-therapy.
Additional information: Presence of granular lymphocytes on 1/3 of lymphocytes, notified as probably related to dasatinib, no other indication in medical record.

The reporter considered "granular lymphocytes" not related to bosutinib; related to concomitant dasatinib.

Follow-up (28Sep2023): This is a non-interventional study follow up report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.
Updated information includes: medical history (ongoing chronic myeloid leukemia).

Case Comment: Based on the available information, the Company considers the reported event granular lymphocytes is unrelated to suspect drug bosutinib but more likely related to dasatinib.

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	96.00 kg	02	MAR	2020

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
#2) SPRYCEL (DASATINIB MONOHYDRATE)

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 500 mg, daily	#1) Unknown
#2) UNK	#2) Oral

17. INDICATION(S) FOR USE
#1) Unknown
#2) CML (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 21-MAR-2019 / 30-MAR-2020	#1) 1 year 10 days
#2) 31-MAR-2020 / 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 to Ongoing	Relevant Med History	CML (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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66 Hudson Boulevard East
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Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
PV202300129596

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

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

DATE OF THIS REPORT
28-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 33-year-old male patient received bosutinib (BOSULIF), from 21Mar2019 to 30Mar2020 at 500 mg daily; dasatinib monohydrate (SPRYCEL), since 31Mar2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "CML" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: HEPATIC CYTOLYSIS (non-serious) with onset 02Mar2020, outcome "recovered" (08Jun2020). The action taken for dasatinib monohydrate was dosage not changed.
Additional information: Consultaion of 08Jun2020: no possibility to increase the dosage of the dasatinib monohydrate, Resolution on 08Sep2020; Change of the 50 mg dasatinib monohydrate to 100 mg, hyperferritinemia in the context of cytolysis. Event "hepatic cytolysis" grade 2, reported non-serious, unrelated to study drug bosutinib and related to concomitant dasatinib; in response to the event, action taken was not applicable for bosutinib.

The reporter considered "hepatic cytolysis" not related to bosutinib.

Follow-up (28Sep2023): This is a non-interventional study (Post Authorization Safety Study) follow-up report from the investigator via CRO for protocol B1871047.
Updated information included: medical history (ongoing chronic myeloid leukemia), updated indication of SPRYCEL, and updated onset date of event hepatic cytolysis (02Mar2020, previously reported as 14Apr2020).

Case Comment: Based on the follow up information received, the onset date of event hepatic cytolysis is 02Mar2020. Of not the event recovered; additionally the administration of bosutinib was permanently discontinued on 30Mar2020 and dasatinib monohydrate was started. According to these new information, a contribution of bosutinib (administered from 21Mar2019) to the event 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		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)

Digestive disorders [Functional gastrointestinal 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) 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	CML (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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New York, NY 10001 UNITED STATES
Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
PV202300130373

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

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

DATE OF THIS REPORT
28-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 received bosutinib (BOSULIF), since Mar2020 (ongoing) at 500 mg daily. The patient's relevant medical history included: "CML" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: FUNCTIONAL GASTROINTESTINAL DISORDER (non-serious) with onset Jun2020, outcome "recovering", described as "Digestive disorders". The action taken for bosutinib was dosage not changed.
Additional information: Digestive disorders with diarrhea almost daily. Event Digestive disorders was rated as grade 2. Epigastric pain from 30Nov2020 to Dec2020 was a symptom of event Digestive disorders.

The reporter considered "digestive disorders" related to bosutinib.

Follow-up (28Jul2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from CRO for protocol B1871047.
Updated information included: medical history updated.

Follow-up (28Sep2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from the investigator via the CRO for protocol B1871047.
Updated information includes: grade of event.

Follow-up (12Oct2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from the clinical team in response to query for protocol B1871047.
Updated information includes: symptom under digestive disorders.

Case Comment: The Company cannot completely exclude the possible causality between the reported "digestive disorders" and the administration of bosutinib, based on the reasonable temporal association and the known safety profile of 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		68 Years	Male	84.00 kg	27	DEC	2017

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

ITCHING ANKLES AND HEAD [Pruritus]
BRONCHITIS [Bronchitis]

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) 02-MAY-2017 / 19-MAY-2017

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.
PV202300157689

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 68-year-old male patient received bosutinib (BOSULIF), from 02May2017 to 19May2017 at 300 mg daily. The patient's relevant medical history was not reported.
The following information was reported: PRURITUS (non-serious) with onset 27Dec2017, outcome "recovered" (17Oct2018), described as "ITCHING ANKLES AND HEAD"; BRONCHITIS (non-serious) with onset 07Oct2018, outcome "recovered" (22Oct2018).

Additional information: the patient had no concomitant medications. Itching ankles and head and bronchitis were considered non-serious, rated grade 1.
The reporter considered "itching ankles and head" and "bronchitis" not related to bosutinib.

Follow-up (03Oct2023): This is a non-interventional study follow-up report received from the clinical team. Updated information includes: Bosulif and patient details, and action taken.

Case Comment: Based on the information currently available, the reported "itching ankles and head" and "bronchitis" are considered unrelated to bosutinib and likely represent intercurrent medical conditions. Case will be reassessed once with additional information.

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	64.00 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)

Tremor of hands [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 (Post Authorization Safety Study) received from 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) Oral

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

18. THERAPY DATES(from/to)
#1) 05-SEP-2018 / 12-OCT-2018

19. THERAPY DURATION
#1) 1 month 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

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.
PV202300157729

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

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

DATE OF THIS REPORT
28-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 05Sep2018 to 12Oct2018 at 300 mg daily, oral. The patient's relevant medical history and concomitant medications were not reported. The following information was reported: TREMOR (non-serious) with onset 12Sep2019, outcome "recovered" (11Mar2020), described as "Tremor of hands".
Additional information: The event tremor of hands was rated grade 1. Bosulif at 300 mg daily oral from 05Sep2018 to 12Oct2018 (permanent discontinuation). The action taken for bosutinib was not applicable.

According to the investigator, the event Tremor of hands was unrelated to study drug bosutinib.

Follow-up (03Oct2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from Clinical team.
Updated information included: dosage regimen and action taken of Bosulif added.

Case Comment: Based on the information currently available, the reported "tremor of hands" is considered unrelated to bosutinib. Event likely represents an 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		71 Years	Female	64.00 kg	05	JUN	2019

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

Asthenia [Asthenia]
depressive syndrome [Depression]

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) Oral

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

18. THERAPY DATES(from/to)
#1) 05-SEP-2018 / 12-OCT-2018

19. THERAPY DURATION
#1) 1 month 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

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.
PV202300157798

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

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

DATE OF THIS REPORT
28-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 05Sep2018 to 12Oct2018 at 300 mg daily, oral. The patient's relevant medical history and concomitant medications were not reported. The following information was reported: ASTHENIA (non-serious) with onset 05Jun2019, outcome "recovered" (12Sep2019); DEPRESSION (non-serious) with onset Jul2019, outcome "recovered" (12Sep2019), described as "depressive syndrome".

The reporter considered "asthenia" and "depressive syndrome" not related to bosutinib.

Additional information: Event asthenia was rated grade 1 and event depressive syndrome was rated grade 2. The patient received bosutinib via oral route at 300 mg daily from 05Sep2018 to 12Oct2018 (permanent withdrawn). Action taken was not applicable.

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

Follow-up (03Oct2023): This is a non-interventional study follow up report (Post Authorization Safety Study) received from clinical team following a query.
Updated information included: dosage regimen and action taken of bosutinib added.

Case Comment: Based on the information currently available, the reported "asthenia" and "depressive syndrome" represent intercurrent medical conditions and are unrelated to bosutinib. Of note, "asthenia" onset almost 8 months after 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	Male	Unk	30	MAY	2022

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

right costal pain [Musculoskeletal chest 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) 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) Oral

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

18. THERAPY DATES(from/to)
#1) 14-OCT-2019 / 26-AUG-2021

19. THERAPY DURATION
#1) 1 year 10 months 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) BOSULIF (BOSUTINIB) ; 03-DEC-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	Relevant Med History	Calculus bladder (Calculus bladder)

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.
PV202300158539

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

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

DATE OF THIS REPORT
28-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 73-year-old male patient received bosutinib (BOSULIF), from 14Oct2019 to 26Aug2021 at 300 mg daily, oral. The patient's relevant medical history included: "VESICULAR LITHIASIS" (unspecified if ongoing). Concomitant medication(s) included: BOSULIF oral, start date: 03Dec2021 (ongoing).
The following information was reported: MUSCULOSKELETAL CHEST PAIN (non-serious) with onset 30May2022, outcome "recovered" (14Sep2022), described as "right costal pain". Relevant laboratory tests and procedures are available in the appropriate section.

Additional information: Right costal pain, the patient describes a discreet pain at 3 on the scale of pain, located just below the right anterior costal grill. Given the existence of a vesicular lithiasis, a murphy manoeuvre is realized which is negative. The abdominal palpation is normal. Finally, the frontal radiography is also strictly normal, in particular without pleural effusion. The event costal pain was rated grade 1. After permanent discontinuation in the study, Bosulif was resumed in a new line (long-term follow-up) from 03Dec21 and ongoing in end of study (M36 Long term).

The investigator considered that the event was unrelated to bosutinib or to any concomitant drug.

Follow-up (03Oct2023): This is a non-interventional study follow-up report received from the clinical team reported study product dosing information, dates of therapy, and information regarding resumption of Bosulif.

Follow-up (05Oct2023): This is a non-interventional study follow-up report from the investigational site via CRO. Updated information includes: Concomitant drug Bosulif added. Action taken for suspcet drug Bosutinib was updated to post therapy. Clinical course.

Case Comment: Based on the information available, the reported "right costal pain" is most likely an intercurrent disease and 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		Investigation	normal	
2		Murphy's sign test Negative	negative	
3		Pain assessment	3	
4		X-ray Without pleural effusion	strictly normal	

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	84.00 kg	07	DEC	2017

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

ostial stenosis of the right renal artery [Renal artery stenosis]
NOSE AND THROAT CONGESTION SENSATION [Upper respiratory tract congestion]

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) Bosutinib (BOSUTINIB) Unknown

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) 02-MAY-2017 / 19-MAY-2017

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.
PV202300160638

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

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

DATE OF THIS REPORT
28-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 68-year-old male patient received bosutinib (BOSUTINIB), from 02May2017 to 19May2017 at 300 mg daily. The patient's relevant medical history and concomitant medications were not reported.
The following information was reported: UPPER RESPIRATORY TRACT CONGESTION (non-serious) with onset 07Dec2017, outcome "recovered" (27Dec2017), described as "NOSE AND THROAT CONGESTION SENSATION"; RENAL ARTERY STENOSIS (hospitalization) with onset Oct2018, outcome "recovered" (07Feb2019), described as "ostial stenosis of the right renal artery".
The reporter considered "ostial stenosis of the right renal artery" and "nose and throat congestion sensation" not related to bosutinib.

Additional information: Ostial stenosis of the right renal artery was rated grade 3 and nose and throat congestion sensation was rated grade 2. The site described: Symptoms and signs of lower-extremity edema that led to hospitalization for renal artery angioplasty after investigation (right renal artery ostial stenosis with delayed left kidney parenchymography indicating upstream stenosis).

Follow-up (03Oct2023): This is a non-interventional study follow-up report received from the clinical team. Updated information includes: Bosutinib dose regimen and dates of administration.

Case Comment: Based on available information and in concurrence with the investigator's assessment, the reported "ostial stenosis of the right renal artery" and "nose and throat congestion sensation" were considered intercurrent medical conditions unrelated 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		69 Years	Male	84.00 kg		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
renal insufficiency worsening [Renal impairment]
SCIATICA [Sciatica]

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) Bosutinib (BOSUTINIB) Unknown

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) 02-MAY-2017 / 19-MAY-2017

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	Vascular device user (Vascular device user)

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.
PV202300160664

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

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

NAME AND ADDRESS WITHHELD.

Mfr. Control Number: PV202300160664

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

for protocol B1871047.

A 69-year-old male patient received bosutinib (BOSUTINIB). The patient's relevant medical history included: "stent" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: SCIATICA (non-serious) with onset Sep2019, outcome "recovered" (19Feb2020); RENAL IMPAIRMENT (medically significant) with onset 03Oct2019, outcome "not recovered", described as "renal insufficiency worsening". The patient underwent the following laboratory tests and procedures: Blood creatinine: ranging between grade 3 and 4. The action taken for bosutinib was unknown.

The reporter considered "renal insufficiency worsening" and "sciatica" not related to bosutinib.

Additional information: Sciatica was rated grade 2, renal insufficiency worsening was rated grade 4. The site described renal insufficiency with creatinine clearance ranging between grade 3 and 4.Dialysis plan but at present contraindicated because of an existing stent.

Follow-up (03Oct2023): This is a non-interventional study follow-up report received from the clinical team. Updated information includes: Bosutinib daily dose, therapy dates and action taken updated from "Unknown" to "Post therapy".

Case Comment: Based on the information currently available, the company concurs with the investigator that "renal insufficiency worsening" and "sciatica" are unrelated to bosutinib. These events onset more than 2 years after last dose of bosutinib and represent intercurrent medical conditions.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Blood creatinine	ranging between grade 3 and 4	

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	04	MAR	2021

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

Internal carotid stenosis [Carotid artery stenosis]
Dyslipidemia [Dyslipidaemia]

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) 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) NILOTINIB (NILOTINIB)

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 300 mg, daily	#1) Unknown
#2) UNK	#2) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 24-OCT-2020 / 16-JAN-2021	#1) 2 months 24 days
#2) 04-FEB-2021 / Ongoing	#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 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.
PV202300161405

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-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 for chronic myeloid leukaemia; nilotinib (NILOTINIB), since 04Feb2021 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: CAROTID ARTERY STENOSIS (non-serious) with onset 04Mar2021, outcome "not recovered", described as "Internal carotid stenosis"; DYSLIPIDAEMIA (non-serious) with onset May2021, outcome "not recovered", described as "Dyslipidemia". The action taken for nilotinib was dosage not changed.

CTCAE for both carotid artery stenosis and dyslipidaemia is Grade 2.

The reporter considered "internal carotid stenosis" and "dyslipidemia" not related to bosutinib and related to Nilotinib.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based on the given information, the events carotid artery stenosis and dyslipidaemia are unrelated to the suspect drug bosutinib. In concurrence with the physician-reporter's assessment, the events carotid artery stenosis and dyslipidaemia are more likely due to the other medication nilotinib.

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	64.00 kg	07	NOV	2016

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

Recurrent angioplasties [Angioplasty]
Gastric ulcer [Gastric ulcer]
Right ankle fracture [Ankle fracture]
Eczema on back and arms [Eczema]

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

(Continued on Additional Information Page)

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

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)

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

18. THERAPY DATES(from/to)
#1) 23-MAY-2016 / 13-JUN-2016

19. THERAPY DURATION
#1) 22 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SPRYCEL (DASATINIB MONOHYDRATE) ; 18-JUL-2016 / Ongoing

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

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	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.
PV202300162866

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

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

A 78-year-old male patient received bosutinib (BOSULIF), first regimen from 23May2016 to 13Jun2016 at 200 mg 1x/day and second regimen from 20Jun2016 to 26Jun2016 at 100 mg 1x/day for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: SPRYCEL oral taken for chronic myeloid leukaemia, start date: 18Jul2016 (ongoing).
The following information was reported: ANGIOPLASTY (hospitalization) with onset 07Nov2016, outcome "recovered" (05Apr2017), described as "Recurrent angioplasties"; ECZEMA (non-serious) with onset Jan2017, outcome "recovered" (11Apr2017), described as "Eczema on back and arms"; ANKLE FRACTURE (non-serious) with onset Jan2017, outcome "recovered" (11Apr2017), described as "Right ankle fracture"; GASTRIC ULCER (hospitalization) with onset 02Jun2017, outcome "recovered" (30Aug2017). The patient was hospitalized for angioplasty (start date: Nov2016). Therapeutic measures were taken as a result of angioplasty.

The reporter considered "recurrent angioplasties", "gastric ulcer", "right ankle fracture" and "eczema on back and arms" not related to bosutinib and concomitant drug.

Additional information: Patient was hospitalized in Nov2016 for 3 angioplasties: angioplasty of bisector artery without stent + proximal anterior interventricular artery angioplasty without stent and mean anterior interventricular artery angioplasty without stent. The patient presented with erythematosous plaques in the upper back and arms with moderate pruritus, plaques were eczematized.
Gastric ulcer, grade 2. Right ankle fracture, grade 2. Recurrent angioplasties, grade 3. Eczema on back and arms, grade 1. Bosulif action taken was not applicable. Sprycel action taken was unknown. For events Gastric ulcer, Right ankle fracture and Recurrent angioplasties: Bosulif action taken was not applicable and Sprycel dose was not changed as action taken.

Follow-up (03Oct2023): This is a follow-up from non-interventional study report received from the investigator via the CRO.
Updated information included: dosage regimen, concomitant drug, new events (Right ankle fracture, Recurrent angioplasties, Eczema on back and arms), event seriousness (hospitalization), event grade, treatment, action taken, clinical course, causality assessment.

Case Comment: The reported events, gastric ulcer, eczema, ankle fracture and angioplasty are intercurrent medical conditions and unrelated to the 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	100 mg, 1x/day; Unknown	Chronic myeloid leukemia (Chronic myeloid leukaemia)	20-JUN-2016 / 26-JUN-2016; 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		67 Years	Male	67.00 kg	17	NOV	2022

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

hypokalemia [Hypokalaemia]

Case Description: eOBSERVATIONAL 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) 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) 06-NOV-2019 / 10-AUG-2021

19. THERAPY DURATION
#1) 1 year 9 months 5 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) IMATINIB (IMATINIB) ; 21-DEC-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 leukaemia (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.
PV202300165372

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300165372

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old male patient received bosutinib (BOSULIF), first regimen from 06Nov2019 to 10Aug2021 at 300 mg daily and second regimen from 11Aug2021 to 06Oct2021 at 200 mg daily. The patient's relevant medical history included: "Chronic myeloid leukaemia" (ongoing). Concomitant medication(s) included: IMATINIB oral taken for chronic myeloid leukaemia, start date: 21Dec2021 (ongoing). The following information was reported: HYPOKALAEMIA (non-serious) with onset 17Nov2022, outcome "not recovered", described as "hypokalemia".
Additional information: Event hypokalemia grade 2, non-serious. Action taken was not applicable for bosutinib and dose not changed for imatinib. The reporter considered "hypokalemia" not related concomitant medication.

The reporter considered "hypokalemia" not related to bosutinib or concomitant medication.

Case Comment: Event hypokalemia represents 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	11-AUG-2021 / 06-OCT-2021; 1 month 26 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		66 Years	Male	67.00 kg	29	MAR	2022

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

dyspnea [Dyspnoea]
inappetence [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 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) IMATINIB (IMATINIB)
(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) 300 mg, daily #2) UNK	#1) Unknown #2) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 06-NOV-2019 / 10-AUG-2021 #2) 21-DEC-2021 / Ongoing	#1) 1 year 9 months 5 days #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.
PV202300165373

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300165373

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 66-year-old male patient received bosutinib (BOSULIF), first regimen from 06Nov2019 to 10Aug2021 at 300 mg daily and second regimen from 11Aug2021 to 06Oct2021 at 200 mg daily; imatinib (IMATINIB), since 21Dec2021 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: DYSPNOEA (non-serious) with onset 29Mar2022, outcome "not recovered", described as "dyspnea"; DECREASED APPETITE (non-serious) with onset 29Mar2022, outcome "not recovered", described as "inappetence". The action taken for imatinib was dosage not changed.

The reporter considered "dyspnea" and "inappetence" not related to bosutinib.

Additional information: Event dyspnea grade 1, non-serious, unrelated to study drug or concomitant. Event inappetence grade 1, non-serious, unrelated to study drug, related to concomitant imatinib (dose not changed).

Follow-up attempts are not needed. No further information is expected.

Case Comment: Based on the available information, the Company considers the reported events "dyspnea" and "inappetence" are unrelated to suspect drug bosutinib. A contributory role of anti-cancer therapy imatinib may provide alternative explanation.

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	11-AUG-2021 / 06-OCT-2021; 1 month 26 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	Male	67.00 kg		MAY	2021

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

asthenia [Asthenia]
SKIN LESIONS OF THE FOREHEAD AND SCALP [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

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) 06-NOV-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) CANDESARTAN (CANDESARTAN) ; Ongoing
#2) EZETROL (EZETIMIBE) ; Ongoing
#3) BISOPROLOL (BISOPROLOL) ; 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 leukaemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
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24b. MFR CONTROL NO.
PV202300165375

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

26. REMARKS

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 male patient received bosutinib (BOSULIF), since 06Nov2019 (ongoing) at 300 mg 1x/day. The patient's relevant medical history included: "Chronic myeloid leukaemia" (ongoing). Concomitant medication(s) included: CANDESARTAN oral taken for hypertension (ongoing); EZETROL oral taken for hypertension (ongoing); BISOPROLOL oral taken for hypertension (ongoing).
The following information was reported: SKIN LESION (non-serious) with onset May2021, outcome "recovered" (10Aug2021), described as "SKIN LESIONS OF THE FOREHEAD AND SCALP"; ASTHENIA (non-serious) with onset May2021, outcome "recovered" (09Nov2021). The action taken for bosutinib was dosage not changed.
Event "SKIN LESIONS OF THE FOREHEAD AND SCALP" grade 1, non-serious, unrelated to study drug or concomitant
Event "asthenia" grade 1, non-serious, related to Bosulif and unrelated to concomitant medication
The reporter considered "asthenia" related to bosutinib. The reporter considered "skin lesions of the forehead and scalp" not related to 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 asthenia and bosutinib cannot be excluded due to plausible temporal association and known drug safety profile. The Company considers the reported event skin lesions of the forehead and scalp 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 Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	FRANCE		PRIVACY		66 Years	Male	67.00 kg		MAY	2021

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

HYPOSIDEREMIA [Iron deficiency]
decrease in breath sounds [Breath sounds abnormal]

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 Physician and an 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) 06-NOV-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 to Ongoing	Relevant Med History	Chronic myelogenous leukemia (Chronic myeloid leukaemia)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Pfizer Inc
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Phone: 212 733 4045

26. REMARKS

24b. MFR CONTROL NO.
PV202300165379

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

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

DATE OF THIS REPORT
28-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 male patient received bosutinib (BOSULIF), since 06Nov2019 (ongoing) at 300 mg daily. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: IRON DEFICIENCY (non-serious) with onset May2021, outcome "recovered" (09Nov2021), described as "HYPOSIDEREMIA"; BREATH SOUNDS ABNORMAL (non-serious) with onset 10Aug2021, outcome "recovered" (29Mar2022), described as "decrease in breath sounds". The action taken for bosutinib was dosage not changed.

The reporter considered Both events grade 1, and unrelated to study drug or concomitant.

Follow-up (06Dec2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from a Physician and an Other HCP for protocol B1871047.
Updated information included: Patient's date of birth updated. Events Hyposideremia and Decrease in breath sounds were confirmed as non-serious.

Case Comment: Based on the information currently available, in concurrence with the investigator, the reported "HYPOSIDEREMIA" and "decrease in breath sounds" are unrelated to bosutinib.
Underlying disease and intercurrent medical condition are plausible 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		78 Years	Male	64.00 kg	02	JUN	2017

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

hiatal hernia [Hiatus hernia]
Evolutive esophagitis [Oesophagitis]

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, 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) 23-MAY-2016 / 13-JUN-2016	#1) 22 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SPRYCEL (DASATINIB MONOHYDRATE) ; 18-JUL-2016 / Ongoing

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

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	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.
PV202300165408

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 78-year-old male patient received bosutinib (BOSULIF), first regimen from 23May2016 to 13Jun2016 at 200 mg daily and second regimen from 20Jun2016 to 26Jun2016 at 100 mg daily. The patient's relevant medical history included: "CML" (ongoing).
Concomitant medication(s) included: SPRYCEL oral taken for chronic myeloid leukaemia, start date: 18Jul2016 (ongoing).
The following information was reported: OESOPHAGITIS (hospitalization) with onset 02Jun2017, outcome "recovered" (30Aug2017), described as "Evolutive esophagitis"; HIATUS HERNIA (hospitalization) with onset 02Jun2017, outcome "recovered" (30Aug2017), described as "hiatal hernia". The patient was hospitalized for hiatus hernia, oesophagitis (hospitalization duration: 2 day(s)). The patient underwent the following laboratory tests and procedures: Endoscopy upper gastrointestinal tract: Result not provided.

Additional information: The action taken in response to both events was reported as not applicable for bosulif and dose not changed for sprycel. The patient had an hospitalization of a 48 -hour duration for gastroscopy.

The reporter considered "hiatal hernia" and "evolutive esophagitis" not related to bosutinib and unrelated to concomitant drug.

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

Case Comment: Both reported hiatus hernia and oesophagitis are considered unrelated to the study drug, bosutinib. Of note, both events developed more than 11 months after the last dose of bosutinib.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		Endoscopy upper gastrointestinal tract	Result not provided	

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	100 mg, daily; Unknown	Unknown	20-JUN-2016 / 26-JUN-2016; 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		78 Years	Male	64.00 kg	02	JUN	2017

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

Erosive duodenitis [Erosive duodenitis]

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 reporters (Physician and Other HCP) for protocol B1871047.

A 78-year-old male patient received bosutinib (BOSULIF), first regimen

(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) 23-MAY-2016 / 13-JUN-2016	#1) 22 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) SPRYCEL (DASATINIB MONOHYDRATE) ; 18-JUL-2016 / Ongoing

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

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Relevant Med History	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.
PV202300165540

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

from 23May2016 to 13Jun2016 at 200 mg daily and second regimen from 20Jun2016 to 26Jun2016 at 100 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: SPRYCEL oral taken for chronic myeloid leukaemia, start date: 18Jul2016 (ongoing).
The following information was reported: EROSIVE DUODENITIS (hospitalization) with onset 02Jun2017, outcome "recovered" (30Aug2017).

Additional information: Event rated grade 1 and assessed as unrelated to bosutinib and to concomitant medication.

The reporter considered "erosive duodenitis" not related to bosutinib.

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

Case Comment: The information provided is too limited. Details of hospitalization, laboratory data, treatment and action taken were not reported. The Company concurs with the reporter and does not attribute the event "erosive duodenitis" 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	100 mg, daily; Unknown	Chronic myeloid leukemia (Chronic myeloid leukaemia)	20-JUN-2016 / 26-JUN-2016; 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		59 Years	Male	85.00 kg		FEB	2020

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

Skin and hips cramps [Muscle spasms]
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
#2) IMATINIB (IMATINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days
#2) 14-JAN-2020 / Ongoing	#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.
PV202300168896

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily; imatinib (IMATINIB), since 14Jan2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: MUSCLE SPASMS (non-serious) with onset Feb2020, outcome "recovered" (24Mar2020), described as "Skin and hips cramps"; EYELID OEDEMA (non-serious) with onset 18Feb2020, outcome "recovered" (03Mar2020), described as "eyelid edema". The action taken for imatinib was dosage not changed.

The reporter considered "skin and hips cramps" and "eyelid edema" not related to bosutinib.

Additional Information: The event skin and hips cramps was non-serious, grade 1, unrelated to bosulif and related to concomitant drug IMATINIB. Action taken with bosutinib was not applicable and no action was taken with imatinib.
The event eyelid edema was non-serious, grade 1, unrelated to bosulif and related to concomitant drug IMATINIB. Action taken with bosutinib was not applicable and no action was taken with imatinib.

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

Case Comment: Based on the information available and in concurrence with the investigator, the reported events, "skin and hips cramps" and "eyelid edema", are unrelated to bosutinib but related to imatinib. The events onset 2 months after bosutinib last dose while patient started imatinib on 14Jan2020.

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-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		59 Years	Male	85.00 kg	08	APR	2020

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

DYSPNEA [Dyspnoea]
EPIGASTRALGIA [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 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) IMATINIB (IMATINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days
#2) 14-JAN-2020 / Ongoing	#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.
PV202300168909

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300168909

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily for chronic myeloid leukaemia; imatinib (IMATINIB), since 14Jan2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: DYSPNOEA (non-serious) with onset 08Apr2020, outcome "recovered" (20Apr2020), described as "DYSPNEA"; ABDOMINAL PAIN UPPER (non-serious) with onset 08Apr2020, outcome "recovered" (20Apr2020), described as "EPIGASTRALGIA". The action taken for imatinib was dosage not changed.

Additional information: dyspnea was grade 1. The event epigastralgia was rated grade 2.

The reporter considered "dyspnea" and "epigastralgia" not related to bosutinib but related to imatinib.

Follow-up (06Dec2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from CRO. Updated information included: The event epigastralgia was rated grade 2.

Case Comment: Based on the information currently available, considering the absence of a plausible temporal relationship (events occurred more than four months after bosutinib last dose), the reported "dyspnea" and "epigastralgia" are considered unrelated to bosutinib. A contributory role of other suspect medication cannot be completely excluded.

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)	19-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	chronic myeloid leukaemia (Chronic myeloid leukaemia)	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		60 Years	Male	85.00 kg	11	JAN	2021

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

worsening on coxarthrosis [Osteoarthritis]

Case Description: The initial case was missing the following minimum criteria: no event.

(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) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) IMATINIB (IMATINIB) ; 14-JAN-2020 / 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 ()

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.
PV202300168914

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300168914

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Upon receipt of follow-up information on 06Dec2023, 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

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

A 60-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: IMATINIB oral taken for chronic myeloid leukaemia, start date: 14Jan2020 (ongoing).
The following information was reported: OSTEOARTHRITIS (hospitalization) with onset 11Jan2021, outcome "recovered" (Feb2021), described as "worsening on coxarthrosis".

The reporter considered "worsening on coxarthrosis" not related to bosutinib.

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

Case Comment: Based on the limited information available, the known safety profile of the suspect product and in concurrence with the reporter's assessment, the event "worsening on coxarthrosis" is considered an intercurrent medical condition 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	300 mg, daily; Unknown	Unknown	19-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		59 Years	Male	85.00 kg	20	APR	2020

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

Subconjunctival hemorrhage [Conjunctival haemorrhage]
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
#2) IMATINIB (IMATINIB)
(Continued on Additional Information Page)

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) Oral

17. INDICATION(S) FOR USE
#1) Unknown
#2) Acute myeloid leukemia (Acute myeloid leukaemia)

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

18. THERAPY DATES(from/to)
#1) 15-JAN-2019 / 18-FEB-2019
#2) 14-JAN-2020 / Ongoing

19. THERAPY DURATION
#1) 1 month 4 days
#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.
PV202300169049

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300169049

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily; imatinib (IMATINIB), since 14Jan2020 (ongoing) (Batch/Lot number: unknown), oral for acute myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: CONJUNCTIVAL HAEMORRHAGE (non-serious) with onset 20Apr2020, outcome "recovered" (14May2020), described as "Subconjunctival hemorrhage"; COVID-19 (non-serious) with onset 16Dec2021, outcome "recovered" (Dec2021), described as "COVID-19 infection". The action taken for imatinib was dosage not changed.

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

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

Case Comment: Based on the available information, the Company considers the reported events "subconjunctival hemorrhage" and "covid-19 infection" are unrelated to suspect drug bosutinib but more likely inter-current medical conditions.

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-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		58 Years	Male	85.00 kg	15	MAR	2019

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

Increase lipasemia [Lipase increased]
Thoracic pain [Chest 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 a Physician and an 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) IMATINIB (IMATINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days
#2) 14-JAN-2020 / Ongoing	#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.
PV202300169051

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 58-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily; imatinib (IMATINIB), since 14Jan2020 (ongoing)), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: LIPASE INCREASED (non-serious) with onset 15Mar2019, outcome "recovered" (16Apr2019), described as "Increase lipasemia"; CHEST PAIN (non-serious) with onset Jan2020, outcome "recovered" (24Mar2020), described as "Thoracic pain". The action taken for bosutinib and imatinib was dosage not changed.

The reporter considered "increase lipasemia" related to bosutinib. The reporter considered "thoracic pain" not related to bosutinib.

Additional information: Increase lipasemia and thoracic pain were both grade 1. Increase lipasemia was unrelated to concomitant treatment while thoracic pain was related to concomitant imatinib. Action taken with bosutinib: dose not changed in response to lipasemia; NA in response to thoracic pain. Action taken with imatinib in response to thoracic pain: dose not changed.

Follow-up (06Dec2023): This is a non-interventional study follow-up report (Post Authorization Safety Study) received from the investigator via the CRO for protocol B1871047.
Updated information: Event verbatim term updated (Increase lipasemia (previously lipasemia)).

Case Comment: The Company cannot completely exclude the possible causality betweent he reported Increase lipasemia and the administration of bosutinib, based on the reasonable temporal association and considering the known safety profile of the suspect. Conversely, the reported thoracic pain is considered unrelated to bosutinib. Thoracic pain occurred more than 1 month after the last dose of bosutinib, and the patient already switched bosutinib to imatinib.

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-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		59 Years	Male	85.00 kg	18	FEB	2020

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

Increased serum creatinine [Blood creatinine increased]
headaches [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
#2) IMATINIB (IMATINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days
#2) 14-JAN-2020 / Ongoing	#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 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.
PV202300169610

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily; imatinib (IMATINIB), since 14Jan2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). The patient's concomitant medications were not reported. The following information was reported: BLOOD CREATININE INCREASED (non-serious) with onset 18Feb2020, outcome "recovered" (23Jun2020), described as "Increased serum creatinine"; HEADACHE (non-serious) with onset 23Mar2020, outcome "recovered" (14May2020), described as "headaches". The action taken for imatinib was dosage not changed.

The reporter considered "increased serum creatinine" and "headaches" not related to bosutinib.

Additional information: Both events grade 1, non-serious, unrelated to bosulif and related to concomitant IMATINIB.
Follow-up attempts are completed. No further information is expected.

Case Comment: Based upon the available information, the reported events blood creatinine increased and headache are deemed unrelated to bosutinib given lack of drug-event temporal association.
Administration of imatinib is the most plausible explanation for the case.

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-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		59 Years	Male	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)

cough [Cough]
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
#2) IMATINIB (IMATINIB)
(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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 15-JAN-2019 / 18-FEB-2019	#1) 1 month 4 days
#2) 14-JAN-2020 / Ongoing	#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.
PV202300169614

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

Mfr. Control Number: PV202300169614

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 59-year-old male patient received bosutinib (BOSULIF), first regimen from 15Jan2019 to 18Feb2019 at 200 mg daily, second regimen from 19Feb2019 to 13Sep2019 at 300 mg daily and third regimen from 15Oct2019 to 29Nov2019 at 200 mg daily; imatinib (IMATINIB), since 14Jan2020 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: COUGH (non-serious) with onset Jan2020, outcome "recovered" (Jan2020); MYALGIA (non-serious) with onset 04Feb2020, outcome "recovered" (24Mar2020). The action taken for imatinib was dosage not changed.

Additional information: Both events were grade 1, non-serious.

The reporter considered "cough" and "myalgia" not related to bosutinib and related to concomitant imatinib.

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

Case Comment: Based on the information currently available, considering the temporal relationship, the reported "cough" and "myalgia" are considered unrelated to bosutinib. A contributory role of other suspect medication cannot be completely excluded.

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-FEB-2019 / 13-SEP-2019; 6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet; Regimen #3	200 mg, daily; Unknown	Unknown	15-OCT-2019 / 29-NOV-2019; 1 month 15 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		67 Years	Female	98.00 kg	28	MAY	2019

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

Creatinine increased [Blood creatinine increased]
Urea increased [Blood urea 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
#2) IMATINIB (IMATINIB)

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) Oral

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

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

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) 29-APR-2019 / 16-SEP-2020	#1) 1 year 4 months 19 days
#2) 02-FEB-2021 / Ongoing	#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 ()

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.
PV202300170864

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old female patient received bosutinib (BOSULIF), from 29Apr2019 to 16Sep2020 at 200 mg daily for chronic myeloid leukaemia; imatinib (IMATINIB), since 02Feb2021 (ongoing) (Batch/Lot number: unknown), oral for chronic myeloid leukaemia. The patient's relevant medical history included: "chronic myeloid leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: BLOOD CREATININE INCREASED (non-serious) with onset 28May2019, outcome "recovered" (02Mar2023), described as "Creatinine increased"; BLOOD UREA INCREASED (non-serious) with onset 28May2019, outcome "recovered" (26Oct2021), described as "Urea increased". The action taken for imatinib was dosage not changed.
Additional information: Event creatinine increased rated grade 2, event urea increased rated grade 1, both considered non serious. Events assessed as both related to study drug bosutinib, event creatinine increased assessed as related to concomitant drug imatinib, and event urea increased assessed as unrelated to concomitant imatinib.

The reporter considered "creatinine increased" and "urea increased" related to bosutinib.

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

Case Comment: Based on the information currently available, considering the temporal relationship and the known product safety profile, a causal association between bosutinib and the reported "creatinine increased" and "urea increased" 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		67 Years	Female	98.00 kg	30	APR	2019

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

diarrheas [Diarrhoea]
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 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) Chronic myelogenous leukemia (Chronic myeloid leukaemia)

18. THERAPY DATES(from/to)
#1) 29-APR-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 to Ongoing	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.
PV202300170986

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

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

DATE OF THIS REPORT
28-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 67-year-old female patient received bosutinib (BOSULIF), since 29Apr2019 (ongoing) at 200 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myelogenous leukemia" (ongoing). The patient's concomitant medications were not reported.
The following information was reported: WEIGHT INCREASED (non-serious) with onset 30Apr2019, outcome "recovered" (23Jul2019), described as "weight gain"; DIARRHOEA (non-serious) with onset 19May2019, outcome "recovered" (19May2019), described as "diarrheas". The action taken for bosutinib was dosage not changed.

The reporter considered "diarrheas" and "weight gain" not related to bosutinib.

Additional information: Both events reported grade 1, unrelated to study drug or concomitant.

Case Comment: Based on the information currently available, in concurrence with reporting healthcare professional, the events diarrhoea and weight increased are likely intercurrent conditions and are considered unrelated to bosutinib. Of note, diarrhoea occurred 21 days after starting bosutinib, and both events reported to have resolved with no change in bosutinib dose.

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	98.00 kg	07	MAY	2019

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

Anemia [Anaemia]
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) 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) 29-APR-2019 / 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.
PV202300170988

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 67-year-old female patient received bosutinib (BOSULIF), since 29Apr2019 at 200 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: MUSCLE SPASMS (non-serious) with onset 07May2019, outcome "recovered" (21May2019), described as "Cramps"; ANAEMIA (non-serious) with onset 28May2019, outcome "recovered" (27Jun2019), described as "Anemia".
The action taken for bosutinib was dosage not changed.

The reporter considered "anemia" related to bosutinib. The reporter considered "cramps" not related to bosutinib.

Additional information: Anemia and Cramps were rated as grade 1, unrelated to concomitant drug.

Case Comment: Based on known drug safety profile, there is reasonable possibility of causal association between the event anemia and the suspect drug bosutinib. Based on available information and as the dose of the suspect drug was not changed, the reported cramps is more likely an intercurrent condition, thus considered 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		69 Years	Female	98.00 kg	04	MAY	2021

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

Muscular cramps [Muscle spasms]
Arterial hypertension flare-up [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) 200 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) 29-APR-2019 / 16-SEP-2020

19. THERAPY DURATION
#1) 1 year 4 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) IMATINIB (IMATINIB) ; 02-FEB-2021 / 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	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.
PV202300171085

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

NAME AND ADDRESS WITHHELD.

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

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

DATE OF THIS REPORT
28-FEB-2024

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

A 69-year-old female patient received bosutinib (BOSULIF), from 29Apr2019 to 16Sep2020 at 200 mg daily for chronic myeloid leukaemia. The patient's relevant medical history included: "Chronic myeloid leukemia" (ongoing). Concomitant medication(s) included: IMATINIB oral taken for chronic myeloid leukaemia, start date: 02Feb2021.
The following information was reported: HYPERTENSION (non-serious) with onset 04May2021, outcome "recovered" (04May2021), described as "Arterial hypertension flare-up"; MUSCLE SPASMS (non-serious) with onset 04May2021, outcome "recovered" (03Aug2021), described as "Muscular cramps".

The reporter considered "muscular cramps" related to bosutinib. The reporter considered "arterial hypertension flare-up" not related to bosutinib.

Additional information: Muscular cramps was grade 1, related to study drug and unrelated to concomitant treatment. Arterial hypertension flare-up was grade 2, unrelated to study drug or concomitant treatment. Action taken was NA.

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

Case Comment: Based on the temporal relationship and/or known AE profile of bosutinib, the reasonable possibility of an association between "muscular cramps", "arterial hypertension flare-up" and suspect product cannot be ruled out.