				CIOMS FOR
SUSPECT	ADVERSE RE	EACTION REPOR	RT	
		I DEAC	ו ואסודי	INFORMATION
	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX 3a. WEIGHT 4-6 REACTION ONSET 8-12 CHECK ALL
PRIVACY	FRANCE	PRIVACY Year	57 Years	Female 86.00 Day Month NOV 2016 APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRED left lobe steatotic hep)	PATIENT DIED INVOLVED OR PROLONGED INPATIENT
Case Description: OB UNDER REAL-LIFE (N OF EF	FICACY AND SAFETY OF BOSULIF HOSPITALISATION INVOLVED PERSISTENT
This is a non-interven protocol B1871047.	porter(s) (Physician and Other HCP) for OR SIGNIFICANT DISABILITY OR INCAPACITY			
A 57-year-old female	(Continued on Additional Information Page)			
	G(S) INFORMATION			
14. SUSPECT DRUG(S) (incluent of the substitution of the substitut	20. DID REACTION ABATE AFTER STOPPING DRUG?			
15. DAILY DOSE(S) #1) UNK	ROUTE(S) OF ADMINISTRATION 1) Unknown			
17. INDICATION(S) FOR USE #1) Unknown	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?			
18. THERAPY DATES(from/to) #1) Unknown				. THERAPY DURATION 1) Unknown YES NO NA
		III. CONCOMITA	ANT DE	RUG(S) AND HISTORY
22. CONCOMITANT DRUG(S)	AND DATES OF ADMINI			
23. OTHER RELEVANT HISTO From/To Dates Unknown	DRY. (e.g. diagnostics, alle	ergies, pregnancy with last mon Type of History / Notes		etc.) Description
Olikilowii				
		IV/ MANUIT/	\CTUD	ED INFORMATION
24a. NAME AND ADDRESS OF	F MANUFACTURER	IV. MANUFA	ACTUR	ER INFORMATION 26. REMARKS
Pfizer Inc Stella Pietrafesa				
66 Hudson Boulevard I New York, NY 10001 U Phone: 212 733 4045				
	24b. MFR CONT	ROL NO.		25b. NAME AND ADDRESS OF REPORTER
	PV2023000			NAME AND ADDRESS WITHHELD.
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SO			NAME AND ADDRESS WITHHELD.
22-FEB-2023	STUDY HEALTH PROFESSIO	LITERATURE ONAL OTHER:		
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TY			

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.

			CIOMS FORM								
SUSPECT AD	VERSE REACTION REPO	RT									
	I. REAG	CTION INFORMATION									
(first, last)	OUNTRY 2. DATE OF BIRTH Day Month Year	2a. AGE 3. SEX 3a. WEIGHT 4-6 REACTION ONSET 54 Link Day Month Yea	8-12 CHECK ALL APPROPRIATE TO								
PRIVACY	ANCE PRIVACY Year	Years Female Unk Day Month NOV 201									
7 + 13 DESCRIBE REACTION(S) (increment Verbatim [PREFERRED TERM	cluding relevant tests/lab data) I] (Related symptoms if any separated by comma:	s)	PATIENT DIED								
Asthenia [Asthenia] Hot flashes [Hot flush]			INVOLVED OR PROLONGED INPATIENT								
	PVATIONAL STUDY - EVALUATIO	ON OF EFFICACY AND SAFETY OF BOSULIF	HOSPITALISATION								
UNDER REAL-LIFE CON		IN OF EFFICACT AND SAFETT OF BOSOLIF	INVOLVED PERSISTENT OR SIGNIFICANT								
		Safety Study) received from contactable reporter	DISABILITY OR INCAPACITY								
(Physician and Other HCF	P) for protocol B1871047.		1_								
		(Continued on Additional Information Page	LIFE THREATENING								
	II. SUSPEC	T DRUG(S) INFORMATION									
			20. DID REACTION ABATE AFTER STOPPING DRUG?								
			DRUG?								
15. DAILY DOSE(S) #1)		16. ROUTE(S) OF ADMINISTRATION #1) Unknown	YES NO NA								
#2) 17. INDICATION(S) FOR USE		#2) Unknown	21. DID REACTION REAPPEAR AFTER								
#1) Unknown #2) Unknown	SUSPECT DRUG(S) (include generic name) 1) Bosulif (BOSUTINIB) Film-coated tablet 2) SPRYCEL (DASATINIB MONOHYDRATE) 1 DAILY DOSE(S) 1 16. ROUTE(S) OF ADMINISTRATION #1) Unknown 2) #2) Unknown 1) Unknown 2) Unknown 1) Unknown										
18. THERAPY DATES(from/to) #1) Unknown			YES NO NA								
#2) Unknown		#2) Unknown									
	III. CONCOMIT	TANT DRUG(S) AND HISTORY									
22. CONCOMITANT DRUG(S) AND I	DATES OF ADMINISTRATION (exclude those use	ed to treat reaction)									
23. OTHER RELEVANT HISTORY. (6 From/To Dates	e.g. diagnostics, allergies, pregnancy with last mo Type of History / Notes	nth of period, etc.) Description									
Unknown											
	D/ 8488 U.E	A OTUBER INFORMATION									
24a. NAME AND ADDRESS OF MAN		ACTURER INFORMATION 26. REMARKS									
Pfizer Inc Stella Pietrafesa											
66 Hudson Boulevard East New York, NY 10001 UNIT											
Phone: 212 733 4045											
	24b. MFR CONTROL NO.	25b. NAME AND ADDRESS OF REPORTER									
	PV202300036698	NAME AND ADDRESS WITHHELD.									
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE STUDY LITERATURE	NAME AND ADDRESS WITHHELD.									
23-FEB-2023	HEALTH OTHER:										
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TYPE INITIAL FOLLOWUP:										

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.

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SUSPECT	SUSPECT ADVERSE REACTION REPORT																
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											\perp	\perp					
		I. REAC	CTION	INFOR	MATION												
PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 71	3. SEX	3a. WEIGHT 2		ACTIO	N ONSE	ET Year	8-12	A	APPF	CK ALL ROPRIA	TE TO			
PRIVACY	TRANCE	PRIVACY	Years	Male	93.00 kg		FEE	3 20	020		F	ADVE	ERSE R	EACI	ION		
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERRE dyspnea [Dyspnoea		tests/lab data) toms if any separated by commas	s)							PATIENT DIED INVOLVED OR							
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE									PROLONGED INPATIENT HOSPITALISATION								
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.									[_	OR S	OLVED F SIGNIFIC BILITY PACITY	CANT OR	STE	NT		
(Continued on Additional Information Page											<u>ا</u> ا	LIFE THRE	EATENII	NG			
		II. SUSPEC	T DRU	G(S) IN	FORMATIO	N											
II. SUSPECT DRUG(S) INFORMATION 14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet													CTION FTER S	TOPF	PING		
15. DAILY DOSE(S)			16		nued on Addition	_	forma	tion P	age	<u>)</u>							
#1) 100 mg, daily				1) Unkno		JIN .						YES	N	> [N/	Α	
17. INDICATION(S) FOR US #1) Unknown	E									21.	REA	PPE	CTION AR AFT DDUCTI				
18. THERAPY DATES(from/t #1) JUN-2019 / Unkr	•			THERAPY 1) Unkno								YES	N	> [3 N≠	Α.	
		III. CONCOMIT	ANT DI	RUG(S	AND HIST	OR	Υ			•							
22. CONCOMITANT DRUG(S) AND DATES OF ADM	INISTRATION (exclude those use	ed to treat rea	action)													
From/To Dates	TORY. (e.g. diagnostics,	allergies, pregnancy with last mor Type of History / Notes		etc.) Description													
Unknown																	
		IV. MANUFA	ACTUR	RER INF	ORMATION	N											
24a. NAME AND ADDRESS Pfizer Inc	OF MANUFACTURER			26. REM													
Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																	
	24b. MFR CO	NTROL NO.		25b. NA	ME AND ADDRESS (OF RE	PORT	ER.			—	—					_
	Ť	PV202300040819 NAME AND ADDRESS WITHHELD.															
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		NAME	AND ADDRES	S W	'ITHH	ELD.									
31-MAR-2023	HEALTH PROFES	ш															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:															

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

							CIOMS FORM
SUSPECT	ADVERSE F	REACTION REPO	RT				
333. 231							
		— I. REA	- CTION	INFOR	MATION		
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT 4	-6 REACTION ONSET	8-12 CHECK ALL APPROPRIATE TO
PRIVACY	FRANCE	PRIVACY Year	64 Years	Male	81.00 Da	y Month Year 2020	ADVEDSE DEACTION
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRE Dyspnea [Dyspnea		tests/lab data) otoms if any separated by comma	as)				PATIENT DIED
Case Description: C UNDER REAL-LIFE		L STUDY - EVALUATIO DF USE	AND SAFETY	OF BOSULIF	PROLONGED INPATIENT HOSPITALISATION		
This is a non-interve reporter(s) (Physicia		oort (Post Authorization 1871047.	ո Safety S	Study) red	eeived from a co	ontactable	INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
				(Cont	inued on Addition	al Information Page)	LIFE THREATENING
		II. SUSPEC	T DRU	G(S) IN	IFORMATIO	N	
14. SUSPECT DRUG(S) (inc #1) Bosulif (BOSUTI	-	tablet					20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) 400 mg, 1x/day				6. ROUTE(S) #1) Unkno) OF ADMINISTRATIO DWN	N	YES NO NA
17. INDICATION(S) FOR US #1) Unknown		21. DID REACTION REAPPEAR AFTER REINTRODUCTION?					
18. THERAPY DATES(from/t #1) 08-SEP-2017 / C				9. THERAPY #1) Unkno			YES NO NA
		III. CONCOMIT	TANT D	RUG(S) AND HIST	ORY	
22. CONCOMITANT DRUG(S) AND DATES OF ADM	IINISTRATION (exclude those us					
23. OTHER RELEVANT HIS From/To Dates Unknown	TORY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes	onth of period	I, etc.) Description			
		IV MANUF	 ACTUF	 PFR IN⊓	FORMATION	J	
24a. NAME AND ADDRESS Pfizer Inc	OF MANUFACTURER	1 7. 100 0 40.	ACTO.	26. REN		\	
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES	3					
	24b. MFR CO	NTROL NO		25b, N/	ME AND ADDRESS O	NE REPORTER	
		00052654			E AND ADDRES		
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE LITERATURE		7			
17-MAR-2023	☑ HEALTH	ш					
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TTYPE FOLLOWUP:					

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.

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SUSPEC	T ADVERSE F	REACTION REPO	RT														
							П						Τ	Τ			
		I DEA	CTION II	NEOD!	MATION	_				ш					1		
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	4-6 RI	EACTIC	N ONS	SET	8-			CK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	69 Years	Male	60.00 tg	Day	Mont AU		Year 201				ROPRIA ERSE R				
7 + 13 DESCRIBE REACTEVENT Verbatim [PREFER depressive syndromes]		tests/lab data) toms if any separated by comma	as)							PATIENT DIED INVOLVED OR PROLONGED INPATIENT							
•	OBSERVATIONAL FE CONDITIONS (_ STUDY- EVALUATIO DF USE	N OF EFF	ICACY A	AND SAFETY	OF I	BOSI	JLIF		PROLONGED INPATIENT HOSPITALISATION							
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.										INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY							
(Continued on Additional Information Page												IFE HRE	EATENI	ING			
II. SUSPECT DRUG(S) INFORMATION																	
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet													CTION FTER S		PPING	1	
15. DAILY DOSE(S) #1) 300 mg, daily	5. DAILY DOSE(S) 16. ROUTE(S) OF ADMINISTRATION											/ES	N	0	X N	A	
17. INDICATION(S) FOR #1) Unknown	USE									21		PPE	CTION AR AFT DDUCT		?		
18. THERAPY DATES(from #1) 03-MAY-2018 /	·			THERAPY) 22 day	DURATION 'S							/ES	N	0 [⊠ N	Ą	
		III. CONCOMI	TANT DR	UG(S	AND HIS	TOR	Υ										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat reac	tion)													
				7													
From/To Dates	IISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes		tc.) escription													
Unknown																	
IV. MANUFACTURER INFORMATION 24a. NAME AND ADDRESS OF MANUFACTURER 26. REMARKS																	_
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																	
	24b. MFR CO	NTROL NO.		25h NA	ME AND ADDRESS	S OF R	PORT	ER									_
	The state of the s	00055947		NAME	AND ADDRE	SS W	/ITHH	ELD.									
24c. DATE RECEIVED BY MANUFACTURER 24d. REPORT SOURCE STUDY LITERATURE NAME AND ADDRESS WITHHELD.																	
23-MAR-2023	HEALTH PROFES	SIONAL OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:															

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.

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SUSPEC	CT ADVERSE F	REACTION REPO	ORT															
							П						Τ					
		I RFA	CTION II	NFOR	MATION													
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT			N ONSE		8-12		ECK ALL PROPRIA		0				
PRIVACY	FRANCE	Day PRIVACY Year	70 Years	Male	60.00 kg	Day 30	OC		Year 2018		AD	VERSE R	≀EAC	TION				
7 + 13 DESCRIBE REAC Event Verbatim [PREFER Right knee wound		tests/lab data) otoms if any separated by comm	as)							PATIENT DIED INVOLVED OR PROLONGED INPATIENT								
•	: OBSERVATIONA FE CONDITIONS (L STUDY- EVALUATIO DF USE	ON OF EFF	CACY A	AND SAFET	Y OF	BOSI	JLIF		PROLONGED INPATIENT HOSPITALISATION								
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.											OR DIS	SIGNIFIO SABILITY CAPACITY	CANT OR					
(Continued on Additional Information Pa												E REATENI	ING					
II. SUSPECT DRUG(S) INFORMATION																		
14. SUSPECT DRUG(S) #1) Bosulif (BOSU					ACTION AFTER S		PING											
5. DAILY DOSE(S) 16. ROUTE(S) OF ADMINISTRATION 11) 300 mg, daily 16. ROUTE(S) OF ADMINISTRATION #1) Unknown											YE	s N	o [2	N/				
17. INDICATION(S) FOR #1) Unknown	USE									1	REAPP	ACTION EAR AFT RODUCT						
18. THERAPY DATES(fro #1) 03-MAY-2018	•			THERAPY) 22 day	DURATION 'S					☐YES ☐ NO 🔲 NA								
		III. CONCOMI	TANT DR	UG(S) AND HIS	STOF	RY											
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	IINISTRATION (exclude those u	sed to treat reac	tion)														
				7														
23. OTHER RELEVANT F	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last m Type of History / Notes														\dashv		
Unknown		Relevant Med Hi		escription imb pro	sthesis user	· (Limb	pros	thesis	s use	er)								
		IV. MANUF	FACTURE	ER INF	ORMATI	ON										_		
Pfizer Inc	SS OF MANUFACTURER			26. REM														
Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																		
	24b. MFR CO	NITPOL NO		25h NAI	ME AND ADDRES	99 OE B	EDODT									\dashv		
		00055952			AND ADDR													
24c. DATE RECEIVED BY MANUFACTURER 24d. REPORT SOURCE STUDY LITERATURE NAME AND ADDRESS WITHHELD.																		
23-MAR-2023	M HEALTH PROFES	ш																
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	TYPE FOLLOWUP:																

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.

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SUSPEC	T ADVERSE F	REACTION REPO	RT				
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		L REΔ		INIEOR	MATION		
1. PATIENT INITIALS	1a. COUNTRY	1. KEA	2a. AGE	3. SEX		4-6 REACTION ONSET	8-12 CHECK ALL
(first, last) PRIVACY	FRANCE	Day PRIVACY Year	64 Years	Male	Unk	Month Year MAR 202	
7 + 13 DESCRIBE REACTI Event Verbatim [PREFERR Other Serious Crite severe hypocalcem	eria: Medically Sig		as)				PATIENT DIED INVOLVED OR PROLONGED INPATIENT
		•	N OF EE	FICACY	AND CAFETY	05 000 III IE	HOSPITALISATION
UNDER REAL-LIF	E CONDITIONS (INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
		oort (Post Authorization P) for protocol B18710		Study) rec	eived from cor	ntactable	
				(Conti	nued on Additio	nal Information Page	LIFE THREATENING
		II. SUSPEC	T DRU	G(S) IN	FORMATIC	DN .	
14. SUSPECT DRUG(S) (in #1) Bosulif (BOSUT	-						20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) UNK				16. ROUTE(S) #1) Unkno	OF ADMINISTRATION	ON	YES NO NA
17. INDICATION(S) FOR U #1) Unknown		21. DID REACTION REAPPEAR AFTER REINTRODUCTION?					
18. THERAPY DATES(from #1) 23-MAY-2019 / 3				19. THERAPY #1) 10 mo	DURATION nths 4 days		YES NO NA
		III. CONCOMIT	TANT D	RUG(S) AND HIST	TORY	
22. CONCOMITANT DRUG	(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat re	eaction)			
	STORY. (e.g. diagnostics,	allergies, pregnancy with last mo	onth of period				
From/To Dates Unknown		Type of History / Notes		Description			
		IV. MANUF	 ACTUI	 RER INF	 ORMATIO	N	
24a. NAME AND ADDRESS Pfizer Inc	S OF MANUFACTURER			26. REM		•	
Stella Pietrafesa 66 Hudson Boulevar New York, NY 1000 Phone: 212 733 404	1 UNITED STATES	3					
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	24b, MFR CO PV20230	ONTROL NO. 00055953			ME AND ADDRESS AND ADDRES	OF REPORTER SS WITHHELD.	
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BY MANUFACTURER 25-JUL-2023	STUDY HEALTH PROFES	LITERATURE SSIONAL OTHER:					
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT						

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.

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SUSPECT	ADVERSE F	REACTION REPO	RT				
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		I RFA	CTION	INFOR	MATION		
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX		REACTION ONSET	8-12 CHECK ALL
PRIVACY	FRANCE	PRIVACY Year	69 Years	Male	60.00 Day kg	Month Year 2018	APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRED constipation [Constip		tests/lab data) toms if any separated by comma	s)				PATIENT DIED INVOLVED OR
Case Description: OE UNDER REAL-LIFE		_ STUDY- EVALUATION OF USE	AND SAFETY O	F BOSULIF	PROLONGED INPATIENT HOSPITALISATION		
		oort (Post Authorization P) for protocol B187104		Study) red	eived from conta	actable	INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
				(Cont	nued on Additiona	I Information Page)	LIFE THREATENING
		II. SUSPEC	T DRU	G(S) IN	FORMATION	 	
14. SUSPECT DRUG(S) (inclu #1) Bosulif (BOSUTIN	-	rablet		·			20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) 300 mg, daily				6. ROUTE(S) #1) Unkno	OF ADMINISTRATION WN		YES NO NA
17. INDICATION(S) FOR USE #1) Unknown							21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
18. THERAPY DATES(from/to) #1) 03-MAY-2018 / 24				9. THERAPY #1) 22 day			YES NO NA
		III. CONCOMIT	TANT D	RUG(S) AND HISTO	PRY	
22. CONCOMITANT DRUG(S)	AND DATES OF ADM	IINISTRATION (exclude those use	ed to treat re	action)			
23. OTHER RELEVANT HISTO From/To Dates Unknown	DRY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes	onth of period	l, etc.) Description			
		IV. MANUF	ACTUE		ORMATION		
24a. NAME AND ADDRESS O Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 I Phone: 212 733 4045	East			26. REM	MARKS		
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24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		NAME	AND ADDRESS	WITHHELD.	
23-MAR-2023	HEALTH PROFES						
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:					

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.

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	1a. COUNTRY		1 1			4-6 RE	ACTION	ONSET	8-1	12 C	HECK /	ALL								
	FRANCE			Male	00.00									l						
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UNDER REAL-LIFE CONDITIONS OF USE This is a non-interventional study report (Post Authorization Safety Study) received from a contactable										OR SIGNIFICANT DISABILITY OR										
eporter(s) (Physician) for protocol B1871047. (Continued on Additional Information Page)												(ae) LIFE THREATENING								
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II. SUSPECT DRUG(S) INFORMATION 14. SUSPECT DRUG(S) (include generic name)													OPPING	6						
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#1) 300 mg, daily #1) Unknown 17. INDICATION(S) FOR USE #1) Unknown 21. DID REACTION REAPPEAR. REINTRODU 18. THERAPY DATES(from/to) 19. THERAPY DURATION]NO	×Ν	A						
		III. CONCOMIT	TANT DE	RUG(S) AND HIS	TOR'	Y		•											
22. CONCOMITANT DRUG	(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat rea	ction)	·															
From/To Dates	STORY. (e.g. diagnostics																			
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24a. NAME AND ADDRESS	S OF MANUFACTURER	IV. MANUF	ACTUR			JN						—								
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	24b. MFR CC	ONTROL NO.			ME AND ADDRES															
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR			\dashv																
BY MANUFACTURER 24-MAR-2023	STUDY HEALTH	LITERATURE																		
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE FOLLOWUP:																		

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.

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<u> </u>					MATION	4				1									
1. PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 70	3. SEX		Day	Monti	1	Year	8-1		APPI	CK ALL ROPRIA ERSE F	ATE		١			
PRIVACY	CTION(C) (including relevant	PRIVACY	Years	Male	kg	21	FEE	3 2	019	<u>'</u>	-								
Event Verbatim [PREFER Pancytopenia [Pa Repeated malais	ancytopenia]	tests/lab data) toms if any separated by comma	as)	PATIENT DIED INVOLVED OR PROLONGED INPATIENT PROSPETALISATION										ENT					
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(Continued on Additional Information Page												LIFE	EATEN	ING					
II. SUSPECT DRUG(S) INFORMATION																			
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15. DAILY DOSE(S) #1) 300 mg, daily #2) 2 DF, daily	#1) 300 mg, daily #1) Unknown #2) 2 DF, daily #2) Unknown												з 🔲 и	0	⊠ \	IA			
17. INDICATION(S) FOR #1) Unknown #2) Unknown	USE									21.	RE/	APPE	CTION EAR AFT ODUCT	TER					
18. THERAPY DATES(fro #1) 02-MAR-2018 #2) 10-AUG-2018	3 / 24-MAY-2018		#	9. THERAPY 1) 2 mon 2) 7 days	ths 23 days							YES	в 🔲 и	0	⊠⊦	IA			
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22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	action)															
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23. OTHER RELEVANT From/To Dates Unknown	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes Relevant Med His since 20-year-old	story	Description	allergy (Dru	g hyp	ersen	sitivit	y)										
		IV. MANUF	ACTUR	RER INF	FORMATIC	ON													
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16-APR-2023	₩ HEALTH PROFES	Ш																	
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	TTYPE FOLLOWUP:																	

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;	

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

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SUSPECT	ADVERSE F	REACTION REPO	RT				
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		I RFA	CTION	INFOR	MATION		
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX		6 REACTION ONSET	8-12 CHECK ALL
PRIVACY	FRANCE	Day PRIVACY Year	69 Years	Male	60.00 Day 03		APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRED anemia [Anaemia]	N(S) (including relevant) TERM] (Related symp	tests/lab data) otoms if any separated by comma	ıs)				PATIENT DIED INVOLVED OR
Case Description: OF UNDER REAL-LIFE		L STUDY- EVALUATION OF USE	N OF EF	FICACY	AND SAFETY C	OF BOSULIF	PROLONGED INPATIENT HOSPITALISATION
		port (Post Authorization P) for protocol B187104	-	Study) red	eived from cont	actable	INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
				(Cont	inued on Addition	al Information Page	LIFE THREATENING
		II. SUSPEC	T DRU	G(S) IN	FORMATIO	N	
14. SUSPECT DRUG(S) (inclu #1) Bosulif (BOSUTIN							20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) 300 mg, daily	N	YES NO NA					
17. INDICATION(S) FOR USE #1) Unknown							21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
18. THERAPY DATES(from/to #1) 03-MAY-2018 / 24	•			19. THERAPY #1) 22 day			YES NO NA
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23. OTHER RELEVANT HISTOFrom/To Dates Unknown	ORY. (e.g. diagnostics,	allergies, pregnancy with last mor Type of History / Notes	onth of period	d, etc.) Description			
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Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES	3					
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24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT			NAME	E AND ADDRESS	S WITHHELD.	
24-MAR-2023	STUDY HEALTH PROFES	SSIONAL DOTHER:					
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT						

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.

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(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	69	Male	60.00 kg	Day 01		onth EB		^{'ear}	1	AF	PPROF	PRIAT		NC		
	TION(S) (including relevant RED TERM] (Related symp eruption [Dermatit	tests/lab data) otoms if any separated by comma is bullous]	as)								[ATIENT VOLVE	ED OF	R			
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		port (Post Authorization P) for protocol B18710		udy) rec	eived from	conta	ctab	le				OF DI:	VOLVE R SIGN SABIL CAPA	NIFICA ITY O	ANT	TEN	Т	
				(Conti	nued on Add	litional	Infor	mati	on Pa	age)	, [FE HREAT	ENIN	IG			
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17. INDICATION(S) FOR #1) Unknown	USE										21.	DID RE REAPI REINT	PEAR	AFTE				
18. THERAPY DATES(fro #1) 21-SEP-2017	•			THERAPY) Unkno	DURATION WN							YE	ES [NO	×	NA		
		III. CONCOMIT	TANT DR	UG(S) AND HI	ISTO	RY											
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23. OTHER RELEVANT H From/To Dates Unknown	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes Relevant Med His	D	escription														
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		IV. MANUF	ACTURE	ER INF	ORMAT	ION												
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25-JUL-2023	HEALTH PROFES	SSIONAL OTHER:																
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	T TYPE																

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;	400 mg, daily; Unknown	Unknown	28-DEC-2017 /
Regimen #2			01-FEB-2018;
			1 month 5 days

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SUSPEC	T ADVERSE F	REACTION REPO	RT																		
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		I. REA	CTION II	NFOR	MATION																
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	2a. AGE 70 Years	3. SEX Male	3a. WEIGHT 60.00 kg	4-6 R	Mont FEI	h	Year 2019	8-1:	Al	HECK PPROI DVERS	PRIAT	E TO ACTIC	N						
Event Verbatim [PREFER	me [Refeeding syn	otoms if any separated by comm	as)							1		ATIEN IVOLV ROLOI OSPIT	ED OF	R INPAT	TENT	г					
UNDER REAL-LII	FE CONDITIONS (JLIF				IVOLV R SIGI ISABIL ICAPA	NIFICA LITY O		ENT						
		oort (Post Authorization P) for protocol B18710									7 u	FE									
				-	nued on Addit		nforma	ation F	Page))	→ TI	HREAT	ENIN	G							
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	T DRUG	(S) IN	FORMATI	ION				120	DID R	EACTI									
	TINIB) Film-coated	tablet						,				E AFTI		OPPIN	IG						
15. DAILY DOSE(S) #1) 300 mg, daily				ROUTE(S)) Unkno	OF ADMINISTRA	TION					ПΥ	ES] NO	×	NA						
17. INDICATION(S) FOR #1) Unknown	USE			REAPP											REACTION APPEAR AFTER INTRODUCTION?						
18. THERAPY DATES(fro #1) 02-MAR-2018	·				DURATION ths 23 days						ПΥ	ES] NO	\boxtimes	NA						
		III. CONCOMI	TANT DR	UG(S) AND HIS	STOF	RY														
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat reac	tion)																	
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23. OTHER RELEVANT F From/To Dates Unknown	IISTORY. (e.g. diagnostics,	allergies, pregnancy with last m Type of History / Notes		tc.) escription																	
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24c. DATE RECEIVED BY MANUFACTURE 24-MAR-2023	R 24d. REPOR' STUDY HEALTH PROFES	LITERATURE		INAIVIE	. AND ADDRI	LUU V	VIIII	ILLU.													
DATE OF THIS REPORT 28-FEB-2024				1																	

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.



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1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	2a. AGE 64 Years	3. SEX Male	3a. WEIGHT Unk	Day 10		onth UG	Y	T /ear 02 1	8-1 1		APPI	CK ALL ROPRIA ERSE R	ATE T			
7 + 13 DESCRIBE REACT Event Verbatim [PREFER Lymphopenia [Lyr Tinnitus [Tinnitus]		tests/lab data) otoms if any separated by comm	as)								1		INVC PRO	ENT DIE	OR :D IN		NT	
	OBSERVATIONAL FE CONDITIONS (L STUDY- EVALUATIO OF USE	ON OF EFF	ICACY A	AND SAFE	TY OF	₹ ВО	SUL	.IF		ו	_ ;	OR S	OLVED F	CANT OR	SISTE T	NT	
		oort (Post Authorization P) for protocol B18710		udy) rec	eived from	conta	ctab	le					LIFE	(PACIT)	Y			
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14. SUSPECT DRUG(S) (include generic name)	II. SUSPEC	CT DRUG	(S) IN	FORMAT	TION					20	חוח	RE^	CTION				
	TINIB) Film-coated	tablet									20.		TE A	FTER S	STOP	PING	i	
15. DAILY DOSE(S) #1) 300 mg, 1x/day	у			ROUTE(S)) Unkno	OF ADMINISTR WN	RATION							YES	□ N	0 [X N	Α	
17. INDICATION(S) FOR #1) Unknown	USE										21.	REA	APPE	CTION AR AFT DDUCT				
18. THERAPY DATES(from #1) 04-JUN-2019 /	•			THERAPY) Unkno	DURATION WN								YES	N	0 [X N	A	
		III. CONCOMI	TANT DR	RUG(S) AND HI	STO	RY											
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat reac	tion)														
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23 OTHER RELEVANT H	IISTORY (e.g. diagnostics	allergies, pregnancy with last m	onth of period e	etc.)														
From/To Dates Unknown		Type of History / Notes		escription														
		IV. MANUF	FACTURI	ER INF	ORMAT	ION												
24a. NAME AND ADDRES Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 40	ard East 01 UNITED STATES	7		26. REM														
	24b. MFR CC	NTROL NO.			ME AND ADDRE													
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24c. DATE RECEIVED BY MANUFACTURE 24-APR-2023	R 24d. REPORT STUDY HEALTH PROFES	LITERATURE		INAIVIE	. AND ADDF	(LOO	VVIII	117E)	∟ ₽.									
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT			1														

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.



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		I. REAC	CTION	INFOR	MATION		7																	
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	-			ON ON:		┥.	12		CK ALI		TO									
PRIVACY	FRANCE	PRIVACY Year	Unk	Male	92.00 Da kg	y	NO		Yea 201				/ERSE			N								
1	TERM] (Related symp	t tests/lab data) ptoms if any separated by commas Imonary arterial hyperte	-	_								INV	IENT D	OR										
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		port (Post Authorization P) for protocol B187104	-	Study) rec	eived from con	tact	able				Ш	OR :	SIGNIF ABILITY APACIT	FICAI Y OR	NT									
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14. SUSPECT DRUG(S) (incli	ude generic name)	II. SUSPEC	IDKU	G(S) IIV	FURIVIATIO	IN				20			ACTION			_								
, ,	11) Bosulif (BOSUTINIB) Film-coated tablet 5. DAILY DOSE(S) 16. ROUTE(S) OF ADMINISTRATION												ABATE AFTER STOPPING DRUG?											
#1) 300 mg, 1x/day				6. ROUTE(S) 41) Unkno		DIN							S			NA								
17. INDICATION(S) FOR USE #1) Unknown										21	RE/	APPE	ACTION EAR AF ODUC	TER										
18. THERAPY DATES(from/to #1) 30-JUN-2016 / 21	•			9. THERAPY t1) 11 mo	DURATION nths 23 days					NA														
		III. CONCOMIT	ANT D	RUG(S	AND HIST	OR	Υ																	
	•	MINISTRATION (exclude those use HYDRATE) ; 10-JUL-2	ed to treat re	action)	,																			
#2) IMATINIB (IMAT			.017 , 32																					
23. OTHER RELEVANT HIST From/To Dates	ORY. (e.g. diagnostics,	allergies, pregnancy with last mor Type of History / Notes		, etc.) Description																				
Unknown to Ongoing		Relevant Med Hist	tory		myeloid leukem	nia (Chro	onic n	nye	loid l	euk	aen	nia)											
24a. NAME AND ADDRESS O	OF MANUFACTURER	IV. MANUFA	ACTUR	26. REM		<u> </u>																		
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	East UNITED STATES	3																						
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25-APR-2023	M HEALTH	ш																						
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE																						

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.

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				7				orma	tion P	age) -	<u> </u>	HRE	ATENI	NG			_					
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	T DRUG	(S) IN	FORMA	TIOI	<u> </u>				20.	DID R											
#1) Bosulif (BOSU #2) SPRYCEL (DA	TINIB) Film-coated											ABAT DRUG		TER S	TOPF	PING							
15. DAILY DOSE(S) #1) 300 mg, daily #2) UNK	DESCRIBE FRANCE Description: ORDER PRANCE Desc													N	> ∑	 NÆ	`						
#1) Unknown	Bosulif (BOSUTINIB) Film-coated tablet SPRYCEL (DASATINIB MONOHYDRATE) ILY DOSE(S) 300 mg, daily JUNK #1) Unknown #2) Oral DICATION(S) FOR USE Jinknown Chronic myelogenous leukemia (Chronic myeloid leukaemia) ERAPY DATES(from/to) 80-JUN-2016 / 21-JUN-2017 #1) 11 months 23 days													21. DID REACTION REAPPEAR AFTER REINTRODUCTION?									
, , , , , , , , , , , , , , , , , , ,	/ 21-JUN-2017		#1) 11 mo	nths 23 day	/S						□ _Y	ſES	□ NO	▷	3 N≠							
		III. CONCOMI	TANT DR	UG(S) AND H	ISTO	OR)	′															
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23. OTHER RELEVANT H From/To Dates Unknown to Ongo		Type of History / Notes	D	escription	myelogend	ous le	uker	mia (Chro	onic	mye	loid I	leul	kaem	nia)								
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24a. NAME AND ADDRE	SS OF MANUFACTURER	IV. WAINOF	AUTUK			IOIV																	
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DATE OF THIS REPORT 28-FEB-2024				1																			

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.

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	ilation [Hypoventila	•	as)								Z ¦	INVO PROL	ENT DIE	OR ED INI		NT	
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				(Cont	nued on Additio	nal In	forma	ation I	Page) [] ¦	LIFE THRE	EATENI	NG			
		II. SUSPEC	CT DRUG	S(S) IN	FORMATIC	N											
14. SUSPECT DRUG(S) (#1) Bosulif (BOSU	include generic name) TINIB) Film-coated	tablet								20.		TE A	CTION FTER S	3TОР	PING	i	
15. DAILY DOSE(S) #1) 300 mg, daily				ROUTE(S)) Unkno	OF ADMINISTRATION	ON						YES	N	o [X N	Ą	
17. INDICATION(S) FOR #1) Unknown	USE									21.	REA	PPE	CTION AR AFT DDUCT				
18. THERAPY DATES(from #1) 30-JUN-2016 /	•				DURATION nths 23 days						□ [,]	YES	N	0 [X N	A	
		III. CONCOMI) AND HIST	ΓOR	Y			•							
	G(S) AND DATES OF ADM ATINIB) ; 28-NO	MINISTRATION (exclude those us V-2018 / Ongoing	sed to treat read	etion)													
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23 OTHER RELEVANT H	IISTORY (a.g. diagnostics	, allergies, pregnancy with last m	onth of period e	atc.)													
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med Hi	D	escription	myelogenous l	leuke	emia	(Chro	onic	mye	loid	leu	kaem	nia)			
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24c. DATE RECEIVED BY MANUFACTURE 25-APR-2023	R 24d. REPOR' STUDY HEALTH	LITERATURE		NAME	E AND ADDRES	SS W	ПHН	ı⊨LD.									
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR																

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 apnea syndrome (start date: 02May2019, discharge date: 03May2019, hospitalization duration: 2 day(s)). Therapeutic measures were taken as a result of sleep apnea 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.

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1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE	3. SEX			EACTIO	ON ONS	SET Year	8-	Α	APPI	CK AL ROPR	RIATE										
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		II. SUSPEC	T DRU	G(S) IN	FORMATIO	N						_												
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet													20. DID REACTION ABATE AFTER STOPPING DRUG?											
15. DAILY DOSE(S) #1) 300 mg/ 200 mg	is. DAILY DOSE(S) 1) 300 mg/ 200 mg alternately 16. ROUTE(S) OF ADMINISTRATION #1) Unknown													YES NO NA										
1 1	17. INDICATION(S) FOR USE #1) Chronic myeloid leukemia (Chronic myeloid leukaemia)													N FTEI CTIO										
18. THERAPY DATES(from/t #1) 31-MAR-2022 / 3	•			9. THERAPY #1) 3 mon								YES		NO	×	NA								
		III. CONCOMIT	TANT D	RUG(S) AND HIST	OR	RΥ					_		_										
· ·	•	MINISTRATION (exclude those us -JUL-2022 / Ongoing	sed to treat re	action)								_												
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From/To Dates		, allergies, pregnancy with last mo Type of History / Notes		Description		_					_	-	-	-	_	=	_							
Unknown to Ongoin	9	Relevant Med His	story	Chronic	myeloid leuken	nia ((Chro	nic m	ıyeı	oid i	euka	em	ıia)											
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24a. NAME AND ADDRESS Pfizer Inc	OF MANUFACTURER	171.111.1121	7.0.0.	26. REM		•																		
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES	S																						
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DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE																						

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 .

				CIOMS FORM					
SUSPECT	ADVERSE REACTION	REPORT							
000. 20.	ADVENUE NEADING.	ILLI OIL.							
		DEACTION	INFORMATION						
1. PATIENT INITIALS	1a. COUNTRY 2. DATE OF		3. SEX 3a. WEIGHT 4-6 REACTION ONSET	8-12 CHECK ALL					
(first, last) PRIVACY	FRANCE Day Month PRIVA	CY Year 78 Years	Female 52.10 Day Month 14 FEB 2023	APPROPRIATE TO ADVERSE REACTION					
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERRE	N(S) (including relevant tests/lab data) D TERM] (Related symptoms if any separate	ed by commas)		PATIENT DIED					
flu syndrom [Influen: lower limb edema [C	za]			INVOLVED OR PROLONGED INPATIENT HOSPITALISATION					
		'ALUATION OF E	FFICACY AND SAFETY OF BOSULIF						
UNDER REAL-LIFE	CONDITIONS OF USE			INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY					
	This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.								
reporter(s) (Errysicia	n) for protocor broz 1047.			LIFE					
(Continued on Additional Information Page)									
•	II. Sl	JSPECT DRL	JG(S) INFORMATION						
	14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet								
15. DAILY DOSE(S) #1) 300 mg / 200 mg	YES NO NA								
17. INDICATION(S) FOR USI #1) Unknown	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?								
18. THERAPY DATES(from/tr #1) 30-JUN-2022 / U			19. THERAPY DURATION #1) Unknown	YES NO NA					
			DRUG(S) AND HISTORY	,					
	S) AND DATES OF ADMINISTRATION (excl ASATINIB); 01-JUL-2022 / O		eaction)						
, ,									
	FORY. (e.g. diagnostics, allergies, pregnancy								
From/To Dates Unknown to Ongoin	Type of Histo Relevant	ory / Notes t Med History	Description Chronic myeloid leukemia (Chronic myeloid	id leukaemia)					
		 MANUFACTU	RER INFORMATION						
24a. NAME AND ADDRESS		777.10	26. REMARKS						
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES								
	24b. MFR CONTROL NO. PV202300084637		25b. NAME AND ADDRESS OF REPORTER NAME AND ADDRESS WITHHELD.						
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE								
10-MAY-2023		ERATURE HER:							
DATE OF THIS REPORT	25a. REPORT TYPE								
28-FEB-2024	28-FEB-2024 INITIAL FOLLOWUP:								

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.

							CIOMS FORM		
SUSPEC	T ADVERSE F	REACTION REPO	RT						
		 I. REA	CTION I	NFOR	MATION				
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	1-6 REACTION ONSET	8-12 CHECK ALL APPROPRIATE TO		
PRIVACY	FRANCE	PRIVACY Year	60 Years	Male	104.00 Da kg	Month Yea 202	ADVEDSE DEACTION		
7 + 13 DESCRIBE REACT Event Verbatim [PREFERF cervical and peri-a		tests/lab data) stoms if any separated by comma	as)				PATIENT DIED INVOLVED OR PROLONGED INPATIENT		
Case Description: UNDER REAL-LIF		L STUDY- EVALUATIO OF USE	N OF EFF	TICACY	AND SAFETY	OF BOSULIF	HOSPITALISATION INVOLVED PERSISTENT		
	This is a non-interventional study report (Post Authorization Safety Study) received from a contactable reporter(s) (Physician) for protocol B1871047.								
	LIFE THREATENING								
II. SUSPECT DRUG(S) INFORMATION									
14. SUSPECT DRUG(S) (i #1) Bosulif (BOSU	20. DID REACTION ABATE AFTER STOPPING DRUG?								
15. DAILY DOSE(S) #1) 300 mg, daily	YES NO NA								
17. INDICATION(S) FOR U #1) Unknown	17. INDICATION(S) FOR USE #1) Unknown								
18. THERAPY DATES(fror #1) 11-MAY-2018 /	·			. THERAPY	DURATION DWN		YES NO NA		
		III. CONCOMIT) AND HIST	ORY			
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat read	ction)					
From/To Dates	ISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo Type of History / Notes		etc.) Description	_				
Unknown									
		D/ MANUE	-^ OT I ID	בט ועוו		. 1			
24a. NAME AND ADDRES	SS OF MANUFACTURER	IV. MANUF	ACTUR	26. REN	FORMATION MARKS	<u>V</u>			
New York, NY 1000									
	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDRESS (OF REPORTER			
	PV20230	00084640		NAME	AND ADDRES	S WITHHELD.			
24c. DATE RECEIVED BY MANUFACTURES	24d. REPORT	SOURCE LITERATURE		7					
17-JUL-2023	M HEALTH PROFES								
DATE OF THIS REPORT 28-FEB-2024									

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.



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SUSPE	CT ADVERSE F	REACTION REPO	RT												_				1
						Т	Τ				T	Т	Т	Τ	Τ	Т	Τ	Τ	┨
							И								l				
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION 2a, AGE	INFOR 3. SEX	MATION 3a. WEIGHT	4.6.5	REACT	TON	ONCE		T _{o 4}		CHE	CK ALL	_				7
PRIVACY	FRANCE	Day Month Year PRIVACY	78	Female	52.10 kg	Day	_	onth	Y	Year 022	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION								
HIATAL HERNIA		tests/lab data) toms if any separated by comma sion]	as)								PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION								
	: OBSERVATIONAL FE CONDITIONS (L STUDY- EVALUATIO DF USE	N OF EFF	FICACY	AND SAFET	TY OF	во	SUL	.IF		ן (□ ;	INVO	OLVED SIGNIFI ABILITY	PER	RSISTI NT	ENT		
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.											_	INCA	APACIT						
(Continued on Additional Information Pag									age)			LIFE	EATEN	ING					
		II. SUSPEC	T DRUC	G(S) IN	FORMAT	ION													_
14. SUSPECT DRUG(S) #1) Bosulif (BOSU #2) DASATINIB (I	JTINIB) Film-coated	tablet		(Conti	nued on Addi	itional I	Infori	nati	on Pa	age)			TE A	CTION AFTER		PPIN	G		
15. DAILY DOSE(S) #1) 300 mg, daily #2) UNK			#	s. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRA WN	ATION							YES	N	Ю	×	NA.		
17. INDICATION(S) FOR #1) Unknown #2) CML (Chronic	use : myeloid leukaemia)										21. DID REACTION REAPPEAR AFTER REINTRODUCTION?								
18. THERAPY DATES(fro #1) 08-APR-2021 #2) 01-JUL-2022	/ 30-MAR-2022		#-	. THERAPY 1) 11 mo 2) Unkno	nths 23 days	3					YES NO NA								
		III. CONCOMIT	TANT DI	RUG(S) AND HIS	STOR	RY												
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	iction)															
															_				
23. OTHER RELEVANT From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med His		Description	nyeloid leuk	vemia.	(Ch	roni	c m	مامیر	id le	عليد	oom	nia)					
Offichiowit to Offigi	oilig	Relevant Med Fils	story	Cilionic	nyelolu leur	Cillia	(CIII	OIII	Cilly	yelo	iu ie	uno	1611	lla)					
		IV. MANUF	ACTUR	ER IN	ORMATI	ON													_
Pfizer Inc	ESS OF MANUFACTURER			26. REM	IARKS														
Stella Pietrafesa 66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	3																	
	24b. MFR CO	INTROL NO.		25h NA	ME AND ADDRE	SS OF F	REPOR	RTFP	<u> </u>						_				\dashv
		00084709			AND ADDR														
24c. DATE RECEIVED BY MANUFACTURE	ER 24d. REPORT	SOURCE LITERATURE		NAME	AND ADDR	ESS V	VIT⊢	IHE	LD.										
07-SEP-2023	M HEALTH PROFES	Ш																	
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																			

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, alternate day;	Unknown	31-MAR-2022 /
Regimen #2	Oral		30-JUN-2022;
			3 months
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, alternate day;	Unknown	31-MAR-2022 /
Regimen #3	Oral		30-JUN-2022;
			3 months

							CIOMS FORM				
SUSPEC	T ADVERSE F	REACTION REPO	RT								
		L DEAA	OTION	L	AATIONI						
1. PATIENT INITIALS	1a. COUNTRY	I. KEAU	2a, AGE	3. SEX	MATION 3a. WEIGHT	4-6 REACTION ONSET	8-12 CHECK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	77 Years	Male	78.80 kg	Month Year 2022	APPROPRIATE TO ADVERSE REACTION				
Other Serious Crite	eria: Medically Sig sensory axonal ne	uropathy [Axonal neuro					PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION				
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)											
II. SUSPECT DRUG(S) INFORMATION											
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet 20. DID REACTION ABATE AFTER STOPPING DRUG?											
15. DAILY DOSE(S) #1) 300 mg, 1x/day	ON	YES NO NA									
17. INDICATION(S) FOR U #1) Chronic myeloid		c myeloid leukaemia)					21. DID REACTION REAPPEAR AFTER REINTRODUCTION?				
18. THERAPY DATES(from #1) Unknown / 20-C	•			o. THERAPY I			YES NO NA				
		III. CONCOMIT	ANT DI	RUG(S)	AND HIS	TORY					
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	INISTRATION (exclude those use	ed to treat rea	action)							
				7							
23. OTHER RELEVANT HIS From/To Dates Unknown to Ongoin		allergies, pregnancy with last mo Type of History / Notes Relevant Med His		Description	nyeloid leuke	mia (Chronic myelo	oid leukaemia)				
		1\/ \/ \/ \ 1\	V CTI ID	ED INIT		ıNı					
24a. NAME AND ADDRESS	S OF MANUFACTURER	IV. MANUF	ACTUR	26. REM		'IN					
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045											
	24b. MFR CO	NTROL NO.			ME AND ADDRESS						
	PV20230					SS WITHHELD. SS WITHHELD.					
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		INAIVIE	AND ADDKE	OO WITHHELD.					
17-JUL-2023	HEALTH	SIONAL OTHER:									
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:											

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	

													CI	OI	ИS	FO	RM
SUSPECT	Γ ADVERSE F	REACTION REPO	RT														
						_			Τ	П	\neg	\neg	\neg	\top	\top	Т	\top
											Щ						
		I. REA	CTION	INFOR	MATION												
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT			ON ONS		8-			CK AL		TO		
PRIVACY	FRANCE	Day Month Year PRIVACY	70 Years	Male		ay)5	NO		Year 202				ERSE			N	
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRE Right pleural effusion	ED TERM] (Related symp	ptoms if any separated by comma	ıs)	,								INVO	ENT D	OR	: 7.4		
Case Description: CUNDER REAL-LIFE		L STUDY - EVALUATIC OF USE	ON OF E	FFICACY	AND SAFETY	OF	BOS	ULIF	•		_ ·	HOS	DLONG PITALI	PER	TON RSISTI		
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician) for protocol B1871047.										OR S	SIGNIF ABILITY APACIT	FICAN Y OR	NT				
(Continued on Additional Information Page									Page	e) (e	□ ;	LIFE THR	EATEN	NING			
	II. SUSPECT DRUG(S) INFORMATION																
14. SUSPECT DRUG(S) (include generic name) 20. DID REACTION																	
#1) Bosulif (BOSUT #2) DASATINIB (DA 15. DAILY DOSE(S)	•	tablet	1	•	inued on Additio	_	nforma	ation F	Page	=)	ABAT DRU		HIEK	810	PPIN	G	
15. DAILY DOSE(S)								YES NO NA									
17. INDICATION(S) FOR USE #1) Unknown #2) Unknown								21	REA	PPE	CTION EAR AF ODUC	TER					
18. THERAPY DATES(from/ #1) 23-DEC-2018 / U #2) 04-SEP-2020 / O	Unknown		#	19. THERAPY #1) Unkno #2) 2 mon								YES	i 🔲	VO	⊠ •	NA	
		III. CONCOMIT	ΓΑΝΤ D	RUG(S) AND HIST	ΓOF	RY_										
22. CONCOMITANT DRUG((S) AND DATES OF ADM	MINISTRATION (exclude those use	ed to treat re	eaction)								_					
23. OTHER RELEVANT HIS From/To Dates	STORY. (e.g. diagnostics,	, allergies, pregnancy with last mo Type of History / Notes	onth of period	d, etc.) Description								_					
Unknown		Relevant Med His	story	None ()													
														—			
24a. NAME AND ADDRESS	OC MANUICACTURED	IV. MANUF	ACTU	RER INI		N								_			
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001																	
	24b. MFR CO	NTROL NO.		25b. NA	ME AND ADDRESS	OF RI	EPORT	ER				_					
	PV20230	00084724			E AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	T SOURCE		NAME	E AND ADDRES	SS W	/ITHH	IELD.									
07-SEP-2023	HEALTH PROFES																
DATE OF THIS REPORT 25a. REPORT TYPE 25aFEB-2024 SINITIAL FOLLOWUP:																	

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. 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

													CIC	MC	S F	OF	۲M
SUSPEC	T ADVERSE F	REACTION REPO	ORT														
							П		T		П	Т	\top	Т	Π		
													\perp				
			CTION II				5										
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	2a. AGE 77 Years	3. SEX Male	3a. WEIGHT 78.80 kg	Day 01	Mor SE	nth	Ye.	APPROPRIATE TO							
Event Verbatim [PREFER RIGHT KIDNEY E	BENIGN CORTICA	t tests/lab data) ptoms if any separated by comm L CYST [Renal cyst] Diverticulum intestinal]	nas)								PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION						
UNDER REAL-LII	FE CONDITIONS (F		ш	OR S	OLVED F SIGNIFIC ABILITY APACITY	CANT OR	ISTE	NT	
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)																	
14 CHEPEOT PRUGOS	(include generic re)	II. SUSPEC	CT DRUG	S(S) IN	FORMAT	ION				1	חום	DF*	CTION				
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(Include generic name) ITINIB) Film-coated	tablet									ABA		AFTER S	STOPI	PING		
15. DAILY DOSE(S) #1) 300 mg, daily 16. ROUTE(S) OF ADMINISTRATION #1) Unknown										YES	S NO	○ [N/	۸.			
17. INDICATION(S) FOR #1) Unknown	USE									2	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(fro #1) Unknown	m/to)			THERAPY) Unkno	DURATION DWN						YES NO NA						
		III. CONCOMI	TANT DR	RUG(S) AND HIS	STO	RY										
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	MINISTRATION (exclude those u	ised to treat reac	etion)													
From/To Dates		allergies, pregnancy with last m Type of History / Notes	D	escription	الدروا أوأوا ومسا	.amia	(Chr	onio		ام:ما	ر المارة		s:a\				
Unknown to Ongo	oing	Relevant Med Hi	istory C	nronic	myeloid leuł	kemia	(Cnr	onic	mye	eioia i	euk	aem	ııa)				
		IV. MANUI	FACTURI	ER INI	ORMATI	ON											
24a. NAME AND ADDRES	SS OF MANUFACTURER			26. REM													
New York, NY 1000	Stella Pietraresa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																
	24b. MFR CC	NITROL NO		25h NA	ME AND ADDRE	SS OF	PEDOD	TEP									
		00084766			E AND ADDR				D.								
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR	T SOURCE		NAME	AND ADDR	ESS	WITH	HELI	D.								
10-MAY-2023	M HEALTH PROFES																
DATE OF THIS REPORT 28-FEB-2024																	

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.	l ah	Da	ta

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

			CIOMS FORM							
SUSPECT A	DVERSE REACTION REPORT									
	I. REACTIO	ON INFORMATION								
(first, last)	2. DATE OF BIRTH 2a. A. P. A. N.C. P. Day Month Year 75		8-12 CHECK ALL APPROPRIATE TO							
PRIVACY	RANCE PRIVACY Year Year Year Year		ADVERSE REACTION							
7 + 13 DESCRIBE REACTION(S) Event Verbatim [PREFERRED TE	(including relevant tests/lab data) RM] (Related symptoms if any separated by commas)		PATIENT DIED							
Diarrhea [Diarrhoea]			INVOLVED OR PROLONGED INPATIENT							
	ERVATIONAL STUDY- EVALUATION OF	EFFICACY AND SAFETY OF BOSULIF	HOSPITALISATION							
UNDER REAL-LIFE CONDITIONS OF USE INVOLVED PERSISTENT OR SIGNIFICANT										
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)										
II. SUSPECT DRUG(S) INFORMATION										
14. SUSPECT DRUG(S) (include generic name) 20. DID REACTION ABATE AFTER STOPPING										
m / boddiii (bodo i i vib	y i mii oodted tablet	(Continued on Additional Information Page)	DRUG?							
15. DAILY DOSE(S) #1) 300 mg, 1x/day	16. ROUTE(S) OF ADMINISTRATION #1) Unknown	YES NO NA								
17. INDICATION(S) FOR USE		21. DID REACTION REAPPEAR AFTER								
#1) Unknown			REINTRODUCTION?							
18. THERAPY DATES(from/to) #1) 06-JAN-2020 / 16-JA	AN-2020	19. THERAPY DURATION #1) 11 days	YES NO NA							
	III. CONCOMITANT	CDRUG(S) AND HISTORY								
22. CONCOMITANT DRUG(S) AN	ID DATES OF ADMINISTRATION (exclude those used to tre	eat reaction)								
From/To Dates	Y. (e.g. diagnostics, allergies, pregnancy with last month of p Type of History / Notes	Description								
Unknown to Ongoing	Relevant Med History	Chronic myeloid leukemia (Chronic myeloi	d leukaemia)							
	1\/ \$44\$11.154.07	TIDED INCODARATION								
24a. NAME AND ADDRESS OF M		URER INFORMATION 26. REMARKS								
Pfizer Inc Stella Pietrafesa										
66 Hudson Boulevard Ea New York, NY 10001 UN										
Phone: 212 733 4045										
	24b. MFR CONTROL NO.	25b. NAME AND ADDRESS OF REPORTER								
	PV202300084778	NAME AND ADDRESS WITHHELD.								
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE STUDY LITERATURE	NAME AND ADDRESS WITHHELD.								
07-SEP-2023	HEALTH OTHER:									
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TYPE INITIAL FOLLOWUP:									

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. 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

													CIO	ON	IS I	FO	RM
SUSPEC	T ADVERSE F	REACTION REPO	ORT														
							Τ		T	T	Τ	Τ		Τ	Τ		П
								U						\perp			
		1	CTION II				9							_			
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	76 Years	3. SEX Male	3a. WEIGHT 79.00 kg	Day 03		onth OV	_	ear							
Prostatic hypertro	TION(S) (including relevant RED TERM] (Related symphy [Benign prosta [Hepatic steatosis]	otoms if any separated by comm ntic hyperplasia]	aas)								PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION						
Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE This is a perpirate positional attack assets (Post Authorization Safety Study) assets of from controlled.							OR DIS	OLVED SIGNIFI ABILITY APACIT	ICAN 'OR	١T	ENT						
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.						_	livo										
(Continued on Additional Information Page)							ge)		THE	REATEN	ING						
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	CT DRUG	i(S) IN	FORMAT	ION				<u> </u>	20. D	ID RE	ACTION	_			1
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet								A		AFTER		PPING	3				
	15. DAILY DOSE(S) #1) 300 mg, 1x/day 16. ROUTE(S) OF ADMINISTRATION #1) Unknown							YES NO NA									
17. INDICATION(S) FOR USE #1) Unknown							21. DID REACTION REAPPEAR AFTER REINTRODUCTION?										
18. THERAPY DATES(fro #1) Ongoing	m/to)			THERAPY) Unkno	DURATION DWN						YES NO NA						
		III. CONCOMI	TANT DR	RUG(S) AND HIS	STO	RY			•							,
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	MINISTRATION (exclude those u	sed to treat reac	tion)													
				7													
														_			
From/To Dates		allergies, pregnancy with last m Type of History / Notes Relevant Med Hi	D	escription	myoloid loul	komio	(Ch	ronic	m	oloic	4 Ιου	kaar	nia)				
Unknown to Ongo	omg	Relevant Med Hi	isiory C	monic	myeloid leuł	Kemia	ı (Cn	TOTIC	нус	eioic	ı ieu	ıkaeı	ilia)				
		IV. MANUF	FACTURE	ER INF	ORMATI	ON											
24a. NAME AND ADDRES	SS OF MANUFACTURER			26. REN													
Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 40	1 UNITED STATES	S															
	24b. MFR CC PV20230	ONTROL NO. 00085545			ME AND ADDRE				D.								
24c. DATE RECEIVED BY MANUFACTURER 24d. REPORT SOURCE STATION				NAME	AND ADDR	RESS	WITH	HEL	D.								
10-MAY-2023		LITERATURE OTHER:															
10-MAY-2023																	

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	

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SUSPEC	T ADVERSE F	REACTION REPO	RT													
												П	Τ	T		
								<u> </u>				Ш				
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION II	NFORI 3. SEX	MATION 3a. WEIGHT	4-6 RI	FACTIO	ON ONS	FT	8-12	2 CH	HECK AL	_			
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	76	Male	76.00	Day 10	Mont OC	th	Year 2022	APPROPRIATE TO						
	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]						PATIENT DIED INVOLVED OR									
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE							НС	ROLONG OSPITALI VOLVED	ISAT	ION						
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician) for protocol B1871047.								OF DIS	R SIGNIF SABILITY CAPACIT	FICAN Y OR	NT	=IN I				
(Continued on Additional Information Page)							, [☐ LIF	E IREATEN	NING						
		II. SUSPEC	T DRUG	(S) INI	FORMATI	ON										
II. SUSPECT DRUG(S) INFORMATION 14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet									ACTION AFTER ?		PPING	3				
15. DAILY DOSE(S) #1) 300 mg, 1x/day 16. ROUTE(S) OF ADMINISTRATION #1) Unknown							YES NO NA									
17. INDICATION(S) FOR #1) chronic myeloi		c myeloid leukaemia)								21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(fro #1) 01-OCT-2019	·			THERAPY () Unknow						YES NO NA						
		III. CONCOMI	TANT DR	UG(S)	AND HIS	TOR	RY									
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	INISTRATION (exclude those us	sed to treat reac	tion)												
23 OTHER RELEVANT I	HISTORY (a.g. diagnostics	allergies, pregnancy with last m	onth of period e	to)									_			
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med Hi	D	escription	nyeloid leuke	emia ((Chro	nic m	nyelo	oid le	ukae	mia)				
			·				`					,				
24a. NAME AND ADDRES	SS OF MANUEACTURER	IV. MANUF	FACTURE	26. REM		<u>NC</u>										
Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva	ard East 01 UNITED STATES	3		ZO. KLIVI	, and c											
	24b. MFR CC	NTROL NO.		25b. NAM	ME AND ADDRES	S OF RI	EPORT	ER								
		00088166		NAME AND ADDRESS WITHHELD.												
24c. DATE RECEIVED BY MANUFACTURE	R 24d. REPOR	SOURCE LITERATURE		NAME	AND ADDRE	ESS W	/ITHH	IELD.								
24-AUG-2023	M HEALTH PROFES	ш														
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																

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.

							CIOMS FORM	
SUSPEC	T ADVERSE F	REACTION REPO	RT					
					MATION		T	
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	Day Month Year PRIVACY	76 Years	3. SEX Male	76.00 Day 04	Month Year 2022	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION	
7 + 13 DESCRIBE REACT Event Verbatim [PREFERE Ferritin at lower lim prostatism [Prostat	nit [Serum ferritin o	t tests/lab data) otoms if any separated by comma decreased]	as)				PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION	
UNDER REAL-LIF	E CONDITIONS (INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY	
This is a non-intervented Other HCP for prof		oort (Post Authorization	Safety S	Study) rec	eived from a Phy	rsician and an		
	LIFE THREATENING							
		II. SUSPEC	T DRU	G(S) IN	FORMATION		20. DID REACTION	
, , ,	14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet							
15. DAILY DOSE(S) #1) 300 mg, daily				6. ROUTE(S) £1) Unkno	OF ADMINISTRATION OWN		YES NO NA	
17. INDICATION(S) FOR L #1) Unknown	JSE						21. DID REACTION REAPPEAR AFTER REINTRODUCTION?	
18. THERAPY DATES(from #1) 01-OCT-2019 /	•			9. THERAPY 41) Unkno			YES NO NA	
		III. CONCOMIT	TANT D	RUG(S) AND HISTO	RY		
22. CONCOMITANT DRUG	3(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat rea	action)				
23. OTHER RELEVANT HI From/To Dates Unknown to Ongoi		allergies, pregnancy with last mo Type of History / Notes Relevant Med His		Description	myeloid leukemia	a (Chronic myeloi	id leukaemia)	
24a. NAME AND ADDRES	S OF MANUFACTURER	IV. MANUF	ACTUR	26. REN	FORMATION MARKS			
Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 404	1 UNITED STATES	\$						
	24b. MFR CO				ME AND ADDRESS OF			
CA- DATE DECEMEN		00088188			E AND ADDRESS			
24c. DATE RECEIVED BY MANUFACTURES 06-DEC-2023	24d. REPORT STUDY HEALTH PROFES	LITERATURE			.,			
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT							

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	

							CIOMS FORM	
SUSPEC	T ADVERSE I	REACTION REPO	RT					
333. 23	. 7.5 (
		I REΔ	CTION	INFOR	MATION			
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX		1-6 REACTION ONSET	8-12 CHECK ALL	
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	73 Years	Male	90.00 Da	Month Year 2020	APPROPRIATE TO ADVERSE REACTION	
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]							PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION	
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							INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY	
This is a non-interview reporter(s) (Physic								
roponor(o) (i riyolo	LIFE THREATENING							
		II. SUSPEC	T DRUC	G(S) IN	IFORMATIO	N		
14. SUSPECT DRUG(S) (ir #1) Bosulif (BOSUT	-			, ,			20. DID REACTION ABATE AFTER STOPPING	
#1) Bosum (Booo I	in (ib) i iiii ooatea	tubict		(Cont	inued on Addition	nal Information Page)	DRUG?	
15. DAILY DOSE(S) #1) 400 mg, daily								
17. INDICATION(S) FOR USE #1) Unknown							21. DID REACTION REAPPEAR AFTER	
,				47			REINTRODUCTION?	
18. THERAPY DATES(from #1) 27-NOV-2017 /	·				DURATION rs 2 months 1 da	ay	YES NO NA	
		III. CONCOMIT	TANT DE	RUG(S) AND HIST	ORY		
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	ction)	,			
23. OTHER RELEVANT HIS From/To Dates	STORY. (e.g. diagnostics	allergies, pregnancy with last mo		etc.) Description				
Unknown to Ongoi	ng	Relevant Med His			myeloid leuken	nia (Chronic myelo	id leukaemia)	
24a. NAME AND ADDRESS	C OF MANUFACTURED	IV. MANUF	ACTUR	ER IN	FORMATIO!	N		
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 404	rd East 1 UNITED STATE:	S		26. KEI	WAKAS			
	24b. MFR CC	ONTROL NO.			AME AND ADDRESS			
	PV20230	00092644			E AND ADDRES			
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR	T SOURCE LITERATURE		NAMI	E AND ADDRES	O WITHHELD.		
23-MAY-2023	1 —	SSIONAL OTHER:						
DATE OF THIS REPORT 28-FEB-2024	DATE OF THIS REPORT 25a. REPORT TYPE							

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. 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

													CIC	MC	S F	OI	RM
SUSPE	CT ADVERSE I	REACTION REPO	RT									_					
						П		T	П	Т	Т	Т	\top	Т			
							14					\perp					
			CTION	INFOR	MATION	4											
1. PATIENT INITIALS (first, last)	(first, last) FRANCE Day Month Year 54 87 00 Day Month Year							1	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION								
PRIVACY		PRIVACY	Years	Male	kg		JAN	1 2	2022		,,	DVL	NOL II		11011		
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]]	PATIENT DIED INVOLVED OR PROLONGED INPATIENT										
Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE						[¬ ⊪	NVOI	LVED F	PERS	ISTE	NT					
		port (Post Authorization P) for protocol B18710		tudy) rec	eived from cor	ntact	able						BILITY PACITY				
(Continued on Additional Information Page)							_[] ¦	IFE HRE	ATENI	NG						
		II. SUSPEC	T DRU	G(S) IN	FORMATIO	N											
14. SUSPECT DRUG(S) #1) Bosulif (BOSU #2) NILOTINIB (N	JTINIB) Film-coated			, ,	nued on Addition		nforma	ition F	Page)	20.	DID R ABAT DRUG	EAF	TION TER S	торі	PING		
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK			#	6. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRATION	ON				YES NO NA							
17. INDICATION(S) FOR #1) Unknown #2) Chronic myelo		c myeloid leukaemia)								21. DID REACTION REAPPEAR AFTER REINTRODUCTION?							
18. THERAPY DATES(fro #1) 17-OCT-2019 #2) 27-OCT-2021	/ 23-OCT-2019		#	o. THERAPY 1)7 days 2)Unkno	•					YES NO NA							
		III. CONCOMIT	TANT D	RUG(S) AND HIST	OR	Υ										
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	action)													
From/To Dates		, allergies, pregnancy with last mo Type of History / Notes		Description			01		1 -				٠-١				
Unknown to Ongo	oing	Relevant Med His	story	Chronic	myeloid leuken	nıa (Chro	nic m	iyelo	id le	uka	∍mı	a)				
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																	
	24b. MFR CC	ONTROL NO.		25b. NA	ME AND ADDRESS	OF RE	EPORTI	ER									
PV202300092696					NAME AND ADDRESS WITHHELD. NAME AND ADDRESS WITHHELD.												
24c. DATE RECEIVED BY MANUFACTURE	24c. DATE RECEIVED BY MANUFACTURER 24d. REPORT SOURCE STUDY LITERATURE					S W	/ITHH	ELD.									
02-OCT-2023	1 —																
DATE OF THIS REPORT 28-FEB-2024	DATE OF THIS REPORT 25a. REPORT TYPE																

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	24-OCT-2019 /
Regimen #2			MAY-2020;
			Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	MAY-2020 /
Regimen #3			12-APR-2021;
			Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet;	100 mg, daily; Unknown	Unknown	13-APR-2021 /
Regimen #4			12-OCT-2021;
			6 months

				CIOMS FORM			
SUSPECT A	DVERSE REACTION REPOR	₹Т					
	I DEAC		NEODWATION .				
PATIENT INITIALS 1a	I. KEAU COUNTRY 2. DATE OF BIRTH		NFORMATION 3. SEX 3a. WEIGHT 4-6 REACTION ONSET	8-12 CHECK ALL			
(first, last)	RANCE Day Month Year	53	emale Unk Day Month Year 2020	APPROPRIATE TO ADVERSE REACTION			
	(including relevant tests/lab data) RM] (Related symptoms if any separated by commas; AT THE CAROTID LEVEL [Carotid a		rosis]	PATIENT DIED INVOLVED OR			
Case Description: OBS UNDER REAL-LIFE CO	ERVATIONAL STUDY- EVALUATION ONDITIONS OF USE	N OF EFFI	CACY AND SAFETY OF BOSULIF	PROLONGED INPATIENT HOSPITALISATION			
This is a non-intervention reporter(s) (Physician a	OR SIGNIFICANT DISABILITY OR INCAPACITY						
	LIFE THREATENING						
	II. SUSPECT	ΓDRUG	(S) INFORMATION				
14. SUSPECT DRUG(S) (include #1) Bosulif (BOSUTINIB	-			20. DID REACTION ABATE AFTER STOPPING DRUG?			
15. DAILY DOSE(S) #1) 500 mg, daily							
17. INDICATION(S) FOR USE #1) Unknown				21. DID REACTION REAPPEAR AFTER REINTRODUCTION?			
18. THERAPY DATES(from/to) #1) 19-MAR-2019 / 27-F	EB-2020		THERAPY DURATION) 11 months 9 days	YES NO NA			
	III. CONCOMITA	ANT DR	UG(S) AND HISTORY				
	ID DATES OF ADMINISTRATION (exclude those used NIB HYDROCHLORIDE) ;03-MAR-						
			7				
			,				
From/To Dates Unknown to Ongoing	/. (e.g. diagnostics, allergies, pregnancy with last mon Type of History / Notes Relevant Med Hist	D	^{tc.)} secription hronic myeloid leukemia (Chronic myeloi	d leukaemia)			
IV. MANUFACTURER INFORMATION							
24a. NAME AND ADDRESS OF M							
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard Ea New York, NY 10001 UN Phone: 212 733 4045							
	24b. MFR CONTROL NO.		25b. NAME AND ADDRESS OF REPORTER				
	PV202300096932		NAME AND ADDRESS WITHHELD.				
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE STUDY LITERATURE		NAME AND ADDRESS WITHHELD.				
30-MAY-2023 HEALTH OTHER:							
DATE OF THIS REPORT 28-FEB-2024 Initial Followup:							

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	Unknown result	
		doppler done in prevention		

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			OTION!!	L					<u> </u>	Ш					<u> </u>		
1. PATIENT INITIALS	1a. COUNTRY	I. KEA	CTION II	NFOR 3. SEX	MATION 3a. WEIGHT	4-6 RI	EACTIC	N ONS	ET	8-1	12 C	HEC	K ALL	—			
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	1 77	Male	83.00	Day 31	Mont AU(Year 202	1	Α	PPR	OPRIA RSE R	ATE TO			
Event Verbatim [PREFER	TION(S) (including relevant RED TERM] (Related symp Urinary tract infect	as)	PATIENT DIED INVOLVED OR														
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE										Н	IOSF	ONGE	SATIO	N			
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.												OR SI	LVED F GNIFIO BILITY PACITY	CANT OR	ISTE	NT	
(Continued on Additional Information Page									age	<u>,</u> [□ ¦	IFE HRE	ATENI	NG			
		II. SUSPEC	T DRUG	(S) IN	FORMATI	ON				•							
14. SUSPECT DRUG(S) (#1) Bosulif (BOSU				,		20.	DID R ABAT DRU(EAF	TION TER S	STOPI	PING						
15. DAILY DOSE(S) #1) UNK				ROUTE(S)) Unkno	OF ADMINISTRAT WN	ΓΙΟΝ					П	/ES	□ NO	> [N/	A	
17. INDICATION(S) FOR #1) Unknown	USE									21.		PPEA	TION R AFT DUCTI				
18. THERAPY DATES(fro #1) Ongoing		19. THERAPY DURATION #1) Unknown ☐ YES ☐ NO ☒ NA								A							
		III. CONCOMI	TANT DR	RUG(S) AND HIS	TOR	RY										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat reac	tion)													
23. OTHER RELEVANT H	IISTORY. (e.g. diagnostics,	allergies, pregnancy with last me Type of History / Notes		etc.)													
Unknown		typo of fileday, notice	_	Coonpacin													
		IV. MANUF	ACTURI	ER INF	ORMATIC	DN_											
24a. NAME AND ADDRES Pfizer Inc	SS OF MANUFACTURER			26. REM	IARKS												
Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 40	1 UNITED STATES	S															
	24b, MFR CC PV20230	ONTROL NO. 00097660			ME AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR	T SOURCE		NAME	AND ADDRE	SS W	/ITHH	IELD.									
31-MAY-2023	STUDY HEALTH PROFES	ш															
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 Minital Followup:																	

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.

12	l ah	Data

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

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SUSPECT	ADVERSE R	EACTION REPO	RT											
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							14					\perp		
		I. REA	CTION	INFOR	MATION									
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	2a. AGE 75 Years	3. SEX	3a. WEIGHT 96.00 kg	4-6 R Day 15	Month NOV	Year		AF		RIATE	TO CTION	
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERRE] Edematous syndrom Acute renal insufficie	ne [Oedema]	ests/lab data) oms if any separated by comma y injury]	s)] IN	ROLON	D OR	NPATIE ION	NT
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										OF DI	R SIGN	IIFICAN	RSISTE NT	NT
B1871047.	B1871047.													
		II 01/0550	TDDU		nued on Addi		inormati	on Page	<u> </u>	- 11	ikeAl	ENING		
14. SUSPECT DRUG(S) (incl	lude generic name)	II. SUSPEC	ו טאט((S) IN	FORMAI	ION					EACTIO		DE	
#1) Bosulif (BOSUTII	NIB) Film-coated ta	ablet								ABATE DRUG		R STO	PPING	
15. DAILY DOSE(S) #1) 300 mg, daily				s. ROUTE(S) 1) Unkno	OF ADMINISTR	ATION				Y	ES []NO	⊠ N∕	A
17. INDICATION(S) FOR USI #1) Unknown	E								R	REAP		ON AFTER ICTION		
18. THERAPY DATES(from/tr #1) 20-NOV-2019 / U	9. THERAPY DURATION #1) Unknown YES NO								⊠ N∕	A				
		III. CONCOMIT) AND HIS	STOF	RY							
22. CONCOMITANT DRUG(S	S) AND DATES OF ADMI	NISTRATION (exclude those us	ed to treat rea	action)										
				7										
22 OTHER RELEVANT HIS	TORY (a.g. diagnostics, a	llergies, pregnancy with last mo	enth of noriod	oto.)										
From/To Dates Unknown	On. (eg. alagnotics)	Type of History / Notes		Description										
		IV. MANUF	ACTUR	ER INI	FORMATI	ON								
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	East UNITED STATES			26. REM		-								
	24b, MFR CON PV202300				ME AND ADDRE									
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT S	SOURCE LITERATURE												
03-JUL-2023	HEALTH PROFESS													
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:												

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.



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		I DEA	CTION	INIEOD	MATION									_						
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX		4-6 RE	EACTIC	N ONS	SET	8-12 CHECK ALL										
(first, last) PRIVACY	PRIVACY FRANCE Day Month Year 34 Male 122.00 Day Month Year																			
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRE GYNECOLOGICAL MUSCLE PAIN [Myster Pain Pain Pain Pain Pain Pain Pain Pain	PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION																			
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE											OR DIS	OLVED SIGNII SABILIT	FICA TY O	ANT	TEN	Т				
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)																				
		II. SUSPEC	T DRU	G(S) IN	IFORMATIC	N														
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet							20	20. DID REACTION ABATE AFTER STOPPING DRUG?												
15. DAILY DOSE(S) #1) 300 mg, daily 16. ROUTE(S) OF ADMINISTRATION #1) Unknown							☐YES ☐NO 🛛 NA													
17. INDICATION(S) FOR USE #1) Unknown							21	RE	EAPPE	ACTION EAR AI RODUC	FTE									
18. THERAPY DATES(from/t #1) 11-DEC-2018 / C	19. THERAPY #1) Unkno				_	_			YES	s 🔲	NO	×	NA							
		III. CONCOMIT	TANT D	RUG(S	3) AND HIST	ΓOR	Υ													
,		MINISTRATION (exclude those us)		•											_		
#1) ASCIMINIB (AS	CIMINIB) ; U/-	-OCT-2020 / Ongoing																		
	TORY. (e.g. diagnostics		onth of period	d, etc.)																
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) From/To Dates Unknown																				
		IV. MANUF		RFR IN	FORMATIO	N														
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa	OF MANUFACTURER	17. 100 010.	<u> </u>	26. REM		11														
66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES	S																		
	24b. MFR CC	ONTROL NO.		25b. N <i>F</i>	AME AND ADDRESS	OF RI	EPORT	ER						_				_		
	*	00102409		ı	E AND ADDRES															
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR	T SOURCE		NAME	E AND ADDRES	SS W	/ITHH	IELD.												
07-JUN-2023	STUDY HEALTH PROFES																			
DATE OF THIS REPORT 28-FEB-2024	DATE OF THIS REPORT 25a. REPORT TYPE																			

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.



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SUSPECT	ADVERSE R	EACTION REPOR	RT											_			
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						Ц	4				\perp			\perp			
		I. REAC	TION II	NFOR	MATION												
1. PATIENT INITIALS (first, last) PRIVACY 1a. COUNTRY PRIVACY 2. DATE OF BIRTH PRIVACY 2a. AGE 70 Year PRIVACY 3a. WEIGHT 4-6 REACTION ONSET 4-6 REACTION ONSET 4-6 REACTION ONSET 4-70 Year PRIVACY 4-6 REACTION ONSET 4-70 Year PRIVACY 4-70 Year 70 Y									┨	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION							
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]									PATIENT DIED INVOLVED OR PROCIONGED INPATIENT HOSPITALISATION								
Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE									1	ш,	OR S	DLVED SIGNIFI ABILITY APACIT	ICAN 'OR	١T	ENT		
		ort (Post Authorization S P) for protocol B187104		udy) rec	eivea irom con	ilaci	abie				_						
(Continued on Additional Information Page									age	•)		LIFE THR	EATEN	ING			
		II. SUSPECT	DRUG	(S) IN	FORMATIO	N				_							
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet								20	20. DID REACTION ABATE AFTER STOPPING DRUG?								
15. DAILY DOSE(S) #1) 500 mg, daily 16. ROUTE(S) OF ADMINISTRATION #1) Unknown										YES		Ю	×۵	A			
17. INDICATION(S) FOR USE #1) chronic myeloid leukaemia (Chronic myeloid leukaemia)									21	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?							
18. THERAPY DATES(from/to #1) 28-NOV-2017 / O				THERAPY) Unkno							YES NO NA						
		III. CONCOMITA	ANT DR	RUG(S)	AND HIST	OR	Y			•							
22. CONCOMITANT DRUG(S) AND DATES OF ADM	INISTRATION (exclude those used	d to treat reac	tion)													
From/To Dates		allergies, pregnancy with last mont Type of History / Notes	D	escription													
Unknown to Ongoing		Relevant Med Histo	ory C	Chronic r	nyeloid leukae	mıa	(Chr	onic r	nye	eloid	leuk	kae	mıa)				
		IV. MANUFA	CTUR	=R INIE		<u> </u>											
24a. NAME AND ADDRESS C	OF MANUFACTURER	IV. IVIAIVOI A	CION	26. REM		<u> </u>								_			
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045																	
	24b. MFR CO	NTROL NO.			ME AND ADDRESS (_			
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24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE LITERATURE		NAME	AND ADDRES	S W	нН	∟LD.									
20-JUL-2023	HEALTH PROFES	SIONAL OTHER:															
DATE OF THIS REPORT 28-FEB-2024	DATE OF THIS REPORT 25a. REPORT TYPE																

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.

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SUSPECT	ADVERSE R	EACTION REPOR	RT							
										
			г т	NFORMATION						
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	72 Years	3. SEX 3a. WEIGHT 4-6 REACTION	ith Year	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION				
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRED Hearing decreased [tests/lab data) toms if any separated by commas	s)			PATIENT DIED INVOLVED OR				
Case Description: Ol UNDER REAL-LIFE	SULIF	PROLONGED INPATIENT HOSPITALISATION INVOLVED PERSISTENT								
This is a non-interve Physician for protoco	le	OR SIGNIFICANT DISABILITY OR INCAPACITY								
A 72-year-old female patient (unknown if pregnant) received bosutinib (Continued on Additional Information Page)										
		II. SUSPEC	T DRUC	G(S) INFORMATION						
14. SUSPECT DRUG(S) (inclu #1) Bosulif (BOSUTIN	· _	20. DID REACTION ABATE AFTER STOPPING DRUG?								
15. DAILY DOSE(S) #1) 500 mg, 1x/day				ROUTE(S) OF ADMINISTRATION 1) Unknown		YES NO NA				
17. INDICATION(S) FOR USE #1) Unknown						21. DID REACTION REAPPEAR AFTER REINTRODUCTION?				
18. THERAPY DATES(from/to #1) 02-JUL-2018 / Or		YES NO NA								
		III. CONCOMIT	ANT DI	RUG(S) AND HISTORY						
22. CONCOMITANT DRUG(S	S) AND DATES OF ADMII	NISTRATION (exclude those use	ed to treat rea	ction)						
23. OTHER RELEVANT HIST From/To Dates Unknown to Ongoing		allergies, pregnancy with last mor Type of History / Notes Relevant Med Hist		^{etc.)} Description Chronic myeloid leukemia (Chro	onic myeloid	d leukaemia)				
		IV MANUE		ER INFORMATION						
24a. NAME AND ADDRESS O	OF MANUFACTURER	1 v. 1vi/ (1 4 C. /	<u> </u>	26. REMARKS						
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES									
	24b. MFR CON	NTROL NO.		25b. NAME AND ADDRESS OF REPORT	TER					
	PV202300			NAME AND ADDRESS WITH	HELD.					
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT S	SOURCE LITERATURE		7						
08-JUN-2023	HEALTH PROFESS	SIONAL OTHER:								
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:								

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.

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SUSPEC	T ADVERSE R	EACTION REPO	RT											
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[CTION I			- 4			1					
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	71 Years	3. SEX emale	3a. WEIGHT 63.00 kg	4-6 RI Day 11	Month DEC	Year 2018	8-12	APPI	CK ALL ROPRIA ERSE RI		N	
		tests/lab data) toms if any separated by comma disc degeneration]	as)							INVO	ENT DIE)R		
Case Description: UNDER REAL-LIF		. STUDY- EVALUATIO F USE	N OF EFF	ICACY /	AND SAFE	TY OF	BOSUL	IF		HOS	DLONGEI SPITALIS.	ATION		
		ort (Post Authorization P) for protocol B18710		udy) rec	eived from	contac	table		╽┕	OR S	SIGNIFIC ABILITY (APACITY	CANT OR	LINI	
				(Conti	nued on Add	litional lı	nformatio	on Page)		LIFE THR	EATENII	٧G		
		II. SUSPEC	T DRUG	S(S) IN	FORMAT	ΓΙΟΝ								
14. SUSPECT DRUG(S) (i #1) Bosulif (BOSU	-	ablet							AE		CTION AFTER S	TOPPIN	G	
15. DAILY DOSE(S) #1) 500 mg, daily				ROUTE(S)) Unkno	OF ADMINISTF WN	RATION				YES	S NC) 	NΑ	
17. INDICATION(S) FOR L #1) Unknown	JSE								RE	EAPPE	CTION EAR AFTI ODUCTIO			
18. THERAPY DATES(from #1) 02-JUL-2018 /	•			THERAPY) Unkno	DURATION WN					YES	S NO) \	NΑ	
		III. CONCOMIT) AND HI	STOF	RY		•					
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	NISTRATION (exclude those us	sed to treat read	tion)										
OR OTHER RELEVANTURE	IOTODY (II II	W 1												
From/To Dates Unknown to Ongoi		allergies, pregnancy with last mo Type of History / Notes Relevant Med His		escription	myeloid leu	kemia ((Chronic	c myelo	oid leul	kaem	nia)			
		IV. MANUF	ACTUR	ER INF	ORMAT	ION								
24a. NAME AND ADDRES Pfizer Inc	S OF MANUFACTURER	111.11		26. REM										
Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 404	1 UNITED STATES													
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	24b. MFR COI				ME AND ADDRI AND ADDF									
24c. DATE RECEIVED BY MANUFACTURES	24d. REPORT	SOURCE LITERATURE		NAME	AND ADD	RESS W	VITHHEL	_D.						
08-JUN-2023	STUDY HEALTH PROFES	ш												
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:												

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 I2 to I5" 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.

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SUSPE	CT ADVERSE F	REACTION REPO	RT														
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1. PATIENT INITIALS	1a. COUNTRY	I. REAC	CTION 2a, AGE	INFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	ON ON	USET		-12	CHE	CK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	78 Years	Male	83.00 kg	Day 08	Mon MA	th	Ye 202	ar	12	APP	ROPRIA ERSE R	ATE 1			
		tests/lab data) otoms if any separated by comma ency [Chronic kidney d											IENT DIE				
	: OBSERVATIONA FE CONDITIONS (L STUDY- EVALUATION OF USE	N OF EF	FICACY	AND SAFET	Y OF	BOS	ULIF	=		۲	PRC	DLONGE	D IN		NT	
		oort (Post Authorization P) for protocol B187104		study) rec	eived from o	contac	table					OR S	OLVED F SIGNIFIO ABILITY APACITY	CAN OR		NT	
				(Conti	nued on Addit	tional I	nform	ation	ı Paç	je)		LIFE THR	: EATENI	NG			
		II. SUSPEC	T DRU	G(S) IN	FORMAT	ION											
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name) JTINIB) Film-coated	tablet		(Conti	nued on Addit	tional I	nform	ation	ı Paç		AB		ACTION AFTER S	STOF	PPING	i	
15. DAILY DOSE(S) #1) 300 mg, daily				6. ROUTE(S) 1) Unkno	OF ADMINISTRA WN	ATION				YES NO NA							
17. INDICATION(S) FOR #1) chronic myelo	use id leukemia in chron	ic pha		(Conti	nued on Addit	tional I	nform	ation	ı Paç		RE	APPE	CTION EAR AFT ODUCT		?		
18. THERAPY DATES(fro #1) 03-JUL-2019	•			19. THERAPY DURATION #1) 1 year 8 months 5 days										A			
		III. CONCOMIT	ANT D	RUG(S) AND HIS	STOF	RY										
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those use	ed to treat rea	action)													
23 OTHER RELEVANT	HISTORY (e.g. diagnostics	allergies, pregnancy with last mo	onth of period	etc)													_
From/To Dates Unknown Unknown		Type of History / Notes Relevant Med His Relevant Med His	story	Description Creatinin	e high (Bloo lure (Renal t			e inc	crea	sed)							
240 NAME AND ADDRE	SS OF MANUFACTURER	IV. MANUF	ACTUR	26. REN		ON											
Pfizer Inc Stella Pietrafesa 66 Hudson Boulev	ard East 01 UNITED STATES	5		20. REN	IARKS												
	24b, MFR CC PV20230	ONTROL NO.			ME AND ADDRES				D.								
24c. DATE RECEIVED BY MANUFACTURE	Malan	LITERATURE		NAME	AND ADDR	ESS V	VITHE	HELD) .								
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR																

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 / Assess	ment / Notes	Results	Normal High / Low
1	Investigati	on	persisting major molecular response	r
14-19. SUSPECT DRUG(S) conf	tinued		•	
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) File	m-coated tablet;	300 mg, daily; Unknown	chronic myeloid leukemia in	03-JUL-2019 /
Regimen #1			chronic phase (Chronic	07-MAR-2021;
			myeloid leukaemia)	1 year 8 months 5
				days
#1) Bosulif (BOSUTINIB) File	m-coated tablet;	200 mg, daily; Unknown	chronic myeloid leukemia in	08-MAR-2021 /
Regimen #2			chronic phase (Chronic	Ongoing;
			myeloid leukaemia)	Unknown

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							Ц.	4										<u> </u>
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION I	NFOR 3. SEX	MATION 3a. WEIGHT	_	6 DE /	VCTIO	N ONS	PET	T.	12 (CUE	CK ALL				
PRIVACY	FRANCE	Day Month Year PRIVACY	78 Years	Male	83.00 kg	Day	,	Month JAN	1	Year 202	.		APP	ROPRIA ERSE F	ATE 1			
Event Verbatim [PREFER		tests/lab data) otoms if any separated by commo xicity to various agents	•										INVC	ENT DI	OR			
	OBSERVATIONA FE CONDITIONS (ON OF EFF	EFFICACY AND SAFETY OF BOSULIF PROLONGED INPATIENT HOSPITALISATION INVOLVED PERSISTENT														
This is a non-inter reporter(s) (Physic	•	udy) red	eived from	n cont	acta	ble					OR S	SIGNIFI ABILITY APACIT	CAN OR	T	INI			
		(Cont	nued on Ad	lditiona	al Inf	orma	tion	Page	∍)		LIFE THRI	EATEN	ING					
		II. SUSPEC	T DRUG	S(S) IN	FORMA	TIOI	N				•							
#1.) Populif (POSLITINIP) Film gosted tablet											TE A	CTION AFTER S		PPING	i			
15. DAILY DOSE(S) #1) 300 mg, daily #2) UNK			#1) Unkno) Unkno) Unkno		TRATION	٧						YES	s 🔲 N	0	X N	A	
17. INDICATION(S) FOR #1) Unknown #2) hormone-sens		ocarcinoma (Adenocarci	noma)								21	REA	APPE	CTION AR AFT ODUCT	TER	?		
18. THERAPY DATES(fro #1) 07-DEC-2020 #2) 07-JAN-2021 /	/ 07-MAR-2021		#1	19. THERAPY DURATION #1) 3 months 1 day #2) Unknown											Ą			
		III. CONCOMI	TANT DF	RUG(S) AND H	IISTO	OR'	Y										
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat read	etion)														
				7														
23. OTHER RELEVANT F From/To Dates Unknown	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last me Type of History / Notes Relevant Med His		escription	rcinoma (/	Δdenc	ocar	cino	ma)									
		carcinoma of the	prostate tr	eated by	ABIRATE	ERON	IE ar	nd F	IRM	AG	ON s	ince	07	Jan2	021			
Unknown		Relevant Med His	story L	Diabetes	mellitus (Diabe	etes	meii	itus)									
		IV. MANUF	ACTURI	ER INI	ORMAT	ΓΙΟΝ	<u> </u>											
Pfizer Inc	SS OF MANUFACTURER			26. REN	IARKS					_			_		_		_	_
Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 40	1 UNITED STATES	3																
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24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR	SOURCE LITERATURE		NAME	AND ADD	RESS	S WI	THH	ELD.	•								
05-OCT-2023	MHEALTH PROFES	ш																
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	TTYPE FOLLOWUP:																

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. 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

								CIOMS FORM	
SUSPECT	TADVERSE F	REACTION REPO	RT						
		I RFA	CTION I	NFOR	MATION				
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	4-6 REAC	TION ONSET	8-12 CHECK ALL	
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	75 Years	Male	96.00 kg		enth Year 202	APPROPRIATE TO ADVERSE REACTION	
7 + 13 DESCRIBE REACTION Event Verbatim [PREFERRE Thoracic pain [Chester Present Prese		tests/lab data) toms if any separated by comma	as)					PATIENT DIED INVOLVED OR PROLONGED INPATIENT	
Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY O UNDER REAL-LIFE CONDITIONS OF USE								PROLONGED INPATIENT HOSPITALISATION INVOLVED PERSISTENT	
This is a non-interventional study report (Post Authorization Safety Study) received from a contactable Physician for protocol B1871047.								OR SIGNIFICANT DISABILITY OR INCAPACITY	
A 75-year-old male	LIFE								
		II. SUSPEC	T DRUG	S(S) IN	FORMATI	ON			
14. SUSPECT DRUG(S) (inc #1) Bosulif (BOSUT	20. DID REACTION ABATE AFTER STOPPING DRUG?								
15. DAILY DOSE(S) #1) 300 mg									
17. INDICATION(S) FOR US #1) Chronic myeloid		c myeloid leukaemia)						21. DID REACTION REAPPEAR AFTER REINTRODUCTION?	
18. THERAPY DATES(from/ #1) 20-NOV-2019 / (•) Unkno	DURATION DWN			YES NO NA	
		III. CONCOMIT	TANT DF	RUG(S) AND HIS	STORY			
22. CONCOMITANT DRUG((S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat read	etion)					
				7					
				,					
From/To Dates		allergies, pregnancy with last mo		escription					
Unknown to Ongoir	ng	Relevant Med His	story (Chronic	myeloid leuk	emia (Ch	ronic myel	oid leukaemia)	
IV. MANUFACTURER INFORMATION									
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4048	d East UNITED STATES	3		26. REM	MARKS				
	24b. MFR CC PV20230	NTROL NO. 00117157			ME AND ADDRES				
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR	SOURCE LITERATURE							
03-JUL-2023	M HEALTH PROFES								
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TTYPE FOLLOWUP:							

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) PRIVACY FRANCE Day Month PRIVACY FRANCE Day Month PRIVACY 73 Male 100.00 Mg Month Prear Day Month Vear Unk France PRIVACY 74 Tabescribe 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
I. REACTION INFORMATION 1. PATIENT INITIALS (first, last) FRANCE Day Month PRIVACY T+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]
I. REACTION INFORMATION 1. PATIENT INITIALS (first, last) FRANCE Day Month PRIVACY T+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]
1. PATIENT INITIALS (first, last) PRIVACY FRANCE Day Month PRIVACY To any local department of total left knee prosthesis due to arthrosis of the knee [Osteoarthritis] 1a. COUNTRY PRIVACY 1a. COUNTRY PRIVACY 1a. COUNTRY PRIVACY PRIVACY 1a. COUNTRY PRIVACY Prear PROPIGIATE TO APPROPRIATE TO APPROPRIATE TO ADVERSE REACTION PATIENT DIED INVOLVED OR PROLONGED INPATIENT
1. PATIENT INITIALS (first, last) PRIVACY PRIVACY 1a. COUNTRY PRIVACY PRIVACY 1a. COUNTRY PRIVACY PROBLEM 3. SEX PRIST TO ADVERSE REACTION ONSET Day Month Vear Unk Pown Month Vear North Month V
1. PATIENT INITIALS (first, last) PRIVACY FRANCE Day Month PRIVACY To any long relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) PATIENT INITIALS 1a. COUNTRY PRIVACY To any long long long long long long long long
PRIVACY FRANCE Day PRIVACY Prear And Male And
placement of total left knee prosthesis due to arthrosis of the knee [Osteoarthritis]
☐ PROLONGED INPATIENT
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)
II. SUSPECT DRUG(S) INFORMATION
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet 20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) 500 mg, daily 16. ROUTE(S) OF ADMINISTRATION #1) Unknown YES NO NA
17. INDICATION(S) FOR USE #1) Unknown 21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
18. THERAPY DATES(from/to) #1) 08-JUL-2019 / Ongoing 19. THERAPY DURATION #1) Unknown
III. CONCOMITANT DRUG(S) AND HISTORY
22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) From/To Dates Type of History / Notes Description
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
Filolie. 212 733 4040
24b. MFR CONTROL NO. 25b. NAME AND ADDRESS OF REPORTER NAME AND ADDRESS WITHHELD.
24c. DATE RECEIVED BY MANUFACTURER 24d. REPORT SOURCE BY MANUFACTURER A STUDY THEREATURE
31-JUL-2023 STUDY LITERATURE STUDY DITTURE STUDY
DATE OF THIS REPORT 28-FEB-2024 Initial Followup:

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.



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SUSPECT	Γ ADVERSE F	REACTION REPO	RT														
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		I. REA	CTION	INFOR	MATION		7										
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE	3. SEX			EACTIO	ON ONS	SET Year	_		APP	CK AL	IATE			
PRIVACY	FRANCE	PRIVACY	73 Years	Male	100.00 kg	dy	JAI		202			ADV	ERSE/	REA	ACTIO	N	
7 + 13 DESCRIBE REACTION FROM THE PROPERTY OF	ED TERM] (Related symp	t tests/lab data) ptoms if any separated by comma	as)			_						INVO PRO	IENT D OLVED DLONG SPITALI	OR ED I	INPAT	IENT	
Case Description: 0 UNDER REAL-LIFE		L STUDY- EVALUATIO OF USE	N OF EF	FICACY	AND SAFETY	OF I	BOSI	JLIF				OR S	OLVED SIGNIF ABILITY	FICAI Y OR	.NT	ENT	
This is a non-intervereporter(s) (Physicial		port (Post Authorization 31871047.	Safety S	Study) red	ceived from a c	onta	ictabl	е					APACIT	ΓY			
				(Cont	inued on Additio	nal Ir	nforma	ation F	Page	e)	<u> </u>	LIFE THR	REATEN	NING	}		
		II. SUSPEC	T DRU	G(S) IN	IFORMATIC	N											
14. SUSPECT DRUG(S) (ind #1) Bosulif (BOSUT #2) BRILIQUE (TIC/	INIB) Film-coated	tablet						,		20		ATE A	ACTION AFTER		OPPIN	IG	
15. DAILY DOSE(S) #1) 500 mg, 1x/day #2)			#	16. ROUTE(S) #1) Unkno #2) Unkno		ON							1 [NA .	
17. INDICATION(S) FOR US #1) Unknown #2) Unknown										21	REA	APPE	CTION EAR AF ODUC	TER			
18. THERAPY DATES(from/ #1) 08-JUL-2019 / C #2) Unknown			#	19. THERAPY #1) Unkno #2) Unkno	own							YES	1 6	NO	×	NA	
		III. CONCOMIT	TANT D	RUG(S) AND HIST	OR	RY_							_			
22. CONCOMITANT DRUG	(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat re	eaction)	·												
From/To Dates		, allergies, pregnancy with last mo Type of History / Notes		Description													
Unknown to Ongoir	ng	Relevant Med His	story	Chronic	myeloid leuker	mia ((Chro	nic m	nyel	oid le	euka	aem	າia)				
		IV MANUE		PER IN	FORMATIO	NI											
24a. NAME AND ADDRESS	OF MANUFACTURER	IV. WITH VOI	AUTU	26. REN		IN											
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevar New York, NY 10001 Phone: 212 733 404	UNITED STATES	S															
	24b. MFR CC	ONTROL NO.		25b. N/	ME AND ADDRESS	OF RI	EPORT	ER									
		00117253		ı	E AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR	T SOURCE															
03-JUL-2023	HEALTH PROFES	ш															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE															

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.

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SUSPEC	T ADVERSE I	REACTION REPO	RT														
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		I. REA	CTION I	NFOR	MATION												
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT			ON ON	_	_	-12		CK ALL ROPRIA		-0		
PRIVACY	FRANCE	Day Month Year PRIVACY	61 Years	Male		09	Mor DE		Ye: 202				ERSE R				
7 + 13 DESCRIBE REACT Event Verbatim [PREFERF Hypertriglyceridem	RED TERM] (Related sym	ptoms if any separated by comma	s)									INVO	ENT DIE	OR			
Case Description: UNDER REAL-LIF		L STUDY- EVALUATION OF USE	N OF EFF	TICACY	AND SAFET	Y OF	BOS	ULIF	:		_	HOS	DLONGE SPITALIS DLVED F	SATIC	ON		
This is a non-interreporter(s) (Physic		port (Post Authorization 31871047.	Safety St	udy) rec	eived from a	conta	actab	le			Ш	OR S	SIGNIFIC ABILITY APACITY	CANT OR	г		
				(Conti	nued on Addit	ional I	nform	ation	Pag	je)		LIFE THR	EATENII	NG			
L		II. SUSPEC	T DRIIG	7				•		-1				_			_
14. SUSPECT DRUG(S) (i	,		1 DRUC) IIV	IONWATI	OIN				20			CTION	ETOE.	DING		
#1) Bosulif (BOSU #2) LOXEN [NICAF 15. DAILY DOSE(S)	,	tablet HLORIDE] (NICARDIPIN			nued on Addit	_	nform	ation	Paç	je)	DR	RUG?					
#1) UNK, daily #2) UNK			#1) Unkno	wn							YES	S NO	э [X NA	A	
17. INDICATION(S) FOR U #1) Unknown #2) Unknown	JSE									2	RE	APPE	CTION EAR AFT ODUCTI				
18. THERAPY DATES(from #1) 30-JAN-2019 / #2) Ongoing	•		#1	THERAPY) Unkno								YES	S NO	o [X NA	A	
		III. CONCOMIT	ANT DE	RUG(S) AND HIS	STOF	RY										
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	MINISTRATION (exclude those use			,												
	ISTORY. (e.g. diagnostics	, allergies, pregnancy with last mo															
From/To Dates Unknown to Ongo	ing	Type of History / Notes Relevant Med His		Description Acute my	eloid leuken	nia (A	cute	myel	loid	leuk	aen	nia)					
		IV. MANUF	ACTUR			NC								_			
24a. NAME AND ADDRES Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 404	ard East 11 UNITED STATE	S		26. REN	IARKS												
	24b. MFR CO	NTROL NO		25h NA	ME AND ADDRES	S OF P	EPOP.	TFR						_			
	The state of the s	00117254			: AND ADDRE).								
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR																
04-OCT-2023	STUDY STUDY	LITERATURE OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR																

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. 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;	100 mg, daily; Unknown	Unknown	25-SEP-2020 /
Regimen #2			Ongoing;
			Unknown
#2) LOXEN [NICARDIPINE	UNK; Unknown	Unknown	Ongoing;
HYDROCHLORIDE] (NICARDIPINE			Unknown
HYDROCHLORIDE) ; Regimen #1			

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1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	84 Years F	3. SEX Female	3a. WEIGHT 60.00 kg	Day	Month OCT	Year 2018	8-12	APPR	CK ALL OPRIAT ERSE RE		N	
		tests/lab data) toms if any separated by common nary tract infection bac								INVOL	ENT DIE	R		
	OBSERVATIONAL	_ STUDY- EVALUATIO DF USE	N OF EFF	TICACY	AND SAFET	Y OF B	OSULI	F		HOSP	ONGED PITALISA LVED PE	ATION		
		oort (Post Authorization P) for protocol B18710		udy) rec	eived from co	ontacta	ble		╽╙	OR SI DISAE	IGNIFICA BILITY C PACITY	ANT	=IN I	
	_			(Conti	nued on Additi	ional Inf	ormatio	n Page)		LIFE THRE	ATENIN	IG		
		II. SUSPEC	T DRUG	S(S) IN	FORMATI	ON								
14. SUSPECT DRUG(S) (#1) Bosulif (BOSU	(include generic name) ITINIB) Film-coated				nued on Additi		ormatio	n Page)	AB DR	D REAC BATE AF RUG?	CTION FTER ST	ГОРРІМ	3	
15. DAILY DOSE(S) #1) 100 mg, 1x/da	у			ROUTE(S)) Unkno	OF ADMINISTRA WN	TION				YES	NO	\	IA	
17. INDICATION(S) FOR #1) Unknown	USE								RE		CTION AR AFTE DUCTIO			
18. THERAPY DATES(fro #1) 24-JUL-2016 /	•			THERAPY) 7 days						YES	NO	×	IA	
		III. CONCOMI) AND HIS	TOR	Y							
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat read	ction)										
23. OTHER RELEVANT F From/To Dates Unknown	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last m Type of History / Notes Relevant Med His		etc.) Description None ()										
		IV. MANUF	ACTURI	ER INF	ORMATIO	ON.								
Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva	01 UNITED STATES			26. REM										
	24b. MFR CO	NTROL NO.			ME AND ADDRES									
		0119456			AND ADDRE									
24c. DATE RECEIVED BY MANUFACTURE		LITERATURE		INAIVIE	AND ADDKE	-00 WI	HINEL							
04-OCT-2023	HEALTH PROFES			4										
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:												

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. 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

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SUSPEC	CT ADVERSE F	REACTION REPO	RT														
							П		Γ			П	T				
		I RFA	CTION II	NFOR	MATION										1		
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	4-6 R	EACTIO	ON ONS	ET	8-12		HECK ALL		то.			
PRIVACY	FRANCE	PRIVACY Year	67 Years	Male	115.00 kg	Day	Mon		Year 2021	1		OVERSE I			١		
	TION(S) (including relevant RED TERM] (Related symp ravation [Hyperten	tests/lab data) toms if any separated by comma Sion]	as)							3		TIENT DI	OR				
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		oort (Post Authorization P) for protocol B18710		udy) rec	eived from c	ontac	table				OF DI	R SIGNIFI SABILITY CAPACIT	ICAN YOR	NΤ			
				(Conti	nued on Addit	ional I	nform	ation P	•age	, [FE IREATEN	NING				
		II. SUSPEC	T DRUG	(S) IN	FORMATI	ON				-							
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name)			` '						20.		EACTION AFTER		PPIN	3		
	, 				nued on Addit	$\overline{}$	nform	ation F	age	<u>)</u>	DINOC						
15. DAILY DOSE(S) #1) 100 mg, 1x/da	у) Unkno	OF ADMINISTRA WN	TION					Y	ES N	10	×ا	IA		
17. INDICATION(S) FOR #1) Unknown	USE					7				21.	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(fro #1) 02-MAY-2019	•			THERAPY) 7 days	DURATION						YE	ES N	۷0	×۵	IA		
		III. CONCOMIT	TANT DR	UG(S) AND HIS	TOF	RY										
22. CONCOMITANT DRU	IG(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat reac	tion)													
				7													
	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo															
From/To Dates Unknown		Type of History / Notes Relevant Med His		escription lone ()													
		IV. MANUF		ER INIE)NI											
24a. NAME AND ADDRE	SS OF MANUFACTURER	TV. IVIATOR	AOTONI	26. REM		<u> </u>											
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	Jan 1722	NITPOL NO		051	ME AND APPE	20.05.5	EDOS	·FP					_				
1	24b, MFR CC PV20230	NTROL NO. 10119467			ME AND ADDRES AND ADDRE												
24c. DATE RECEIVED BY MANUFACTURE	24d. REPORT	SOURCE LITERATURE		NAME	AND ADDRE	ESS V	VITHE	IELD.									
31-JUL-2023	M HEALTH PROFES	ш															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	TTYPE FOLLOWUP:															

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, 1x/day; Unknown	Unknown	09-MAY-2019 /
Regimen #2			22-MAY-2019;
			14 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, 1x/day; Unknown	Unknown	23-MAY-2019 /
Regimen #3			Ongoing;
			Unknown

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							4					Ш	上			
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION II	NFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	ON ONS	FT	8-12	2 CH	IECK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	63	Male	117.00 kg	Day	Mont FEI	th	Year 2019	1	AP	PROPRIA	ATE TO			
7 + 13 DESCRIBE REAC Event Verbatim [PREFER Asthmatic bronch		tests/lab data) otoms if any separated by comma	as)							5		TIENT DIE	OR			
•	: OBSERVATIONA FE CONDITIONS (L STUDY- EVALUATIC DF USE	ON OF EFF	ICACY	AND SAFET	Y OF	BOSI	ULIF			НО	OLONGE OSPITALIS	SATIO	N		
	rventional study repcian) for protocol B	oort (Post Authorization 1871047.	n Safety Stu	udy) red	eived from o	ontac	table				OR DIS	VOLVED F R SIGNIFIC SABILITY CAPACITY	CANT OR	ISTE	NT	
				(Cont	inued on Addit	tional I	nforma	ation F	Page)	, [E REATENI	ING			
		II. SUSPEC	T DRUG	(S) IN	FORMAT	ION										
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name) JTINIB) Film-coated	tablet			inued on Addit	_	nforma	ation F	Page)			ACTION AFTER S		PING		
15. DAILY DOSE(S) #1) 100 mg, 1x/da	у) Unkno	OF ADMINISTRA OWN	ATION					YE	S N	o [2	N/	۸	
17. INDICATION(S) FOR #1) Unknown	USE									21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(fro #1) 23-NOV-2017	•				DURATION ths 9 days						YE	S NO	o [N/	A.	
		III. CONCOMI	TANT DR	UG(S) AND HIS	STOF	RY									
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	IINISTRATION (exclude those us	sed to treat reac	tion)												
				7												
	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last me														
From/To Dates Unknown to Ongo	ping	Type of History / Notes Relevant Med His		escription Chronic	myeloid leuk	emia	(Chro	nic m	iyeld	oid le	ukae	mia)				
		IV. MANUF		ED INI		ON.										
24a. NAME AND ADDRE	SS OF MANUFACTURER	IV. WANGI	ACTON	26. REN		OIN										
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	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDRES	SS OF R	EPORT	ER					—			
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24c. DATE RECEIVED BY MANUFACTURE	24d. REPORT	SOURCE LITERATURE		NAME	E AND ADDRI	ESS V	VITHH	iELD.								
17-JUL-2023	HEALTH PROFES	SSIONAL OTHER:														
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	T TYPE FOLLOWUP:														

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. 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

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		L DEA	OTIONII	<u> </u>						<u> </u>	Ш							
1. PATIENT INITIALS	1a. COUNTRY	I. REA	2a. AGE	NFOR 3. SEX	MATION 3a. WEIGHT	4-6	REA	CTION	ONS	ET	8-1	12 (CHE	CK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	54 Years F	emale	60.70 kg	Day		Month JAN		Year 202				ROPRIA ERSE R				
7 + 13 DESCRIBE REAC Event Verbatim [PREFER Cruralgia [Sciatica Hernia [Hernia]		t tests/lab data) otoms if any separated by comm	as)								1		NVO	ENT DIE	OR D IN		:NT	
UNDER REAL-LIF	FE CONDITIONS (JLIF		[) –	OR S DISA	LVED F IGNIFIC BILITY PACITY	CANT OR	SISTE T	NT	
		oort (Post Authorization P) for protocol B18710		udy) rec	eived from	conta	actal	ble				'	NCA	FACITI	ı			
				(Conti	nued on Add	litiona	l Info	ormat	ion P	age) [□ ¦	LIFE THRE	EATENI	NG			
		II. SUSPEC	CT DRUG	(S) IN	FORMAT	ΠΟΝ	1				1							
, ,	(include generic name)	tablet	l ia		nued on Add	_	$\overline{}$	ormat	ion P	Page			TE A	CTION FTER S	STOP	PING		
15. DAILY DOSE(S) #1) 200 mg) Unkno	OF ADMINISTR WN	RATION							YES	□ N	0 [N.	A	
17. INDICATION(S) FOR #1) Unknown	USE										21.	REA	PPE	CTION AR AFT DDUCTI		,		
18. THERAPY DATES(fro #1) 05-JAN-2020 /				THERAPY) 7 days	DURATION								YES	N	0 [X N	A	
		III. CONCOMI	TANT DR	RUG(S) AND HI	STC	RY	′										_
	G(S) AND DATES OF ADM NILOTINIB) ; AUG	MINISTRATION (exclude those u G-2020 / Ongoing	sed to treat reac	tion)														
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) From/To Dates Unknown to Ongoing Relevant Med History Chronic myeloid leukemia (Chronic myeloid leukemia)									ıyel	oid le	euka	ıem	ia)					
		IV. MANUF	FACTURE	ER INF	ORMAT	ION												
24a. NAME AND ADDRES Pfizer Inc Stella Pietrafesa 66 Hudson Boulev New York, NY 1000 Phone: 212 733 40	ard East 01 UNITED STATES	3		26. REM	IARKS													
	24b. MFR CO				ME AND ADDRE													\exists
24c. DATE RECEIVED BY MANUFACTURE	24d. REPORT	00125178 I SOURCE			AND ADDF													
BY MANUFACTURE 07-SEP-2023	STUDY HEALTH	LITERATURE OTHER:																
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	T TYPE																

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 leukemia, 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 investigator 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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg; Unknown	Unknown	12-JAN-2020 /
Regimen #2			05-APR-2020;
			2 months 25 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	30-APR-2020 /
Regimen #3			JUN-2020;
			Unknown
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	JUN-2020 /
Regimen #4		7	26-AUG-2020;
			Unknown

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SUSPEC	T ADVERSE F	REACTION REPO	RT														
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		I DEA	CTION II	NEOD	MATION										<u> </u>	Ш	
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	_	REAC	TION	ONSET	г	8-12	CHE	CK ALL				
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	60 Years	Male	104.00 kg	Day 02		lonth	Ye 20	ear 20			PROPRIA /ERSE R				
Event Verbatim [PREFER	FION(S) (including relevant RED TERM] (Related symp ighs folliculitis [Foll	otoms if any separated by comma	as)									I INV	IENT DIE	OR			
•	OBSERVATIONA FE CONDITIONS (L STUDY- EVALUATIC DF USE	ON OF EFF	ICACY /	AND SAFE	TY O	F BO	SUL	.IF			НО	DLONGE SPITALIS	SATIO	N		
		oort (Post Authorization P) for protocol B18710		udy) rec	eived from	conta	actab	le				OR DIS	OLVED F SIGNIFIO ABILITY APACITY	CANT OR		NI	
				(Conti	nued on Add	ditiona	l Infor	rmatio	on Pa	ge)		LIFE	E REATENI	NG			
		II. SUSPEC	T DRUG	i(S) IN	FORMA	TION	1										
14. SUSPECT DRUG(S) (#1) Bosulif (BOSU	include generic name) TINIB) Film-coated	tablet		(Conti	nued on Add	ditiona	l Infor	rmatic	on Pa		A		ACTION AFTER S	ТОР	PING		
15. DAILY DOSE(S) #1) 100 mg) Unkno	OF ADMINISTI WN	RATION						YES	S NO	> [N/	١.	
17. INDICATION(S) FOR #1) Unknown	USE										21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(from #1) 22-APR-2018				THERAPY) 10 day	DURATION 'S							YE	S NO)	N/		
		III. CONCOMI	TANT DR	RUG(S) AND H	ISTC	RY										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	INISTRATION (exclude those us	sed to treat reac	tion)													
23. OTHER RELEVANT H	IISTORY. (e.g. diagnostics,	allergies, pregnancy with last me		etc.)													
Unknown to Ongo	ing	Relevant Med His			myeloid leu	ukemia	a (Ch	nronio	c my	eloid	l leu	kaer	nia)				
		IV. MANUF	ACTUR			ION											
24a. NAME AND ADDRES Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000 Phone: 212 733 40	ard East 01 UNITED STATES	3		26. REM	IARKS												
	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDR	ESS OF	REPO	RTER									_
	PV20230	00125269			AND ADD												
24c. DATE RECEIVED BY MANUFACTURE	R 24d. REPOR	SOURCE LITERATURE		NAME	AND ADD	KESS	WITI	HHEl	_D.								
07-SEP-2023	HEALTH PROFES	SSIONAL OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	TTYPE FOLLOWUP:															

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. 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

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		I. REA	CTION	INFOR	MATION		7										
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE	3. SEX			EACTIC	N ONS	SET Year	8-1	,	APP	CK AL	IATE			
PRIVACY	FRANCE	PRIVACY	78 Years	Male	76.30 kg	ay	JUI		202		,	ADV	ERSE	REA	CTIO	N	
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERRE	N(S) (including relevant D TERM] (Related sym	t tests/lab data) ptoms if any separated by comma	as)									PATI	ENT D	IED			
chronic renal failure diarrhea [Diarrhoea]	. ,	disease]											DLVED LONG			IENT	
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This is a non-interve	entional study re	port (Post Authorization	າ Safety S	Study) rec	ceived from a c	onta	ctabl	e			- 1	DISA	ABILITY APACIT	Y OR			
reporter(s) (Physicia						7											
				(Cont	inued on Addition	nal Ir	nforma	ation I	Page	_{e)}	<u>.</u>	LIFE THR	EATEN	NING	;		
		II. SUSPEC	T DRU	G(S) IN	FORMATIO	N								_			
14. SUSPECT DRUG(S) (inc #1) Bosulif (BOSUTI	-	tablet								20	ABA	TE A	CTION AFTER		DPPIN	IG	
#2) NILOTINIB (NILC	,	tubict						,			DRU	IG?					
15. DAILY DOSE(S) #1) 300 mg, 1x/day #2) UNK			#	6. ROUTE(S) #1) Unkno #2) Oral	OF ADMINISTRATIO	ON						YES	1 🔲	NO	× I	NA	
17. INDICATION(S) FOR US #1) Unknown #2) chronic myeloid I		c myeloid leukaemia)								21	REA	PPE	CTION AR AF ODUC	TER			
18. THERAPY DATES(from/t #1) 24-OCT-2020 / 1 #2) 04-FEB-2021 / O	6-JAN-2021		#	9. THERAPY #1) 2 mon #2) Unkno	ths 24 days							YES	ı 🔲 ı	NO	⊠¹	NA	
		III. CONCOMIT	TANT D	RUG(S) AND HIST	OR	Υ										
22. CONCOMITANT DRUG(S	S) AND DATES OF ADM	MINISTRATION (exclude those us			77		•										
	TORY. (e.g. diagnostics,	, allergies, pregnancy with last mo	onth of period														
From/To Dates Unknown to Ongoin	g	Type of History / Notes Relevant Med His	story	Description Chronic	myeloid leuken	nia ((Chro	nic m	nyel	oid le	euka	ıem	nia)				
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		IV. MANUF	ACTUF		FORMATIO	N								_			
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa	OF MANUFACTURER			26. REN	1ARKS												
66 Hudson Boulevard New York, NY 10001																	
Phone: 212 733 4045		9															
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18-JUL-2023	STUDY HEALTH PROFES	LITERATURE OTHER:															
DATE OF THIS REPORT	25a. REPORT			\dashv													
28-FEB-2024	⊠ INITIAL	FOLLOWUP:															

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.



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1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION II	NFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONSI	ET	8-12	. CH	ECK ALL	_			
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	71	Male	-	Day	Monti SEF	n ,	Year 019	1	AP	PROPRIA VERSE F	ATE T			
7 + 13 DESCRIBE REAC Event Verbatim [PREFER Pneumopathy [Lu Bronchitis [Bronch	ng disorder]	t tests/lab data) otoms if any separated by comm	aas)							[[2]		TIENT DII OLVED (OLONGE SPITALIS	OR ED INF		NT	
UNDER REAL-LII	FE CONDITIONS (JLIF			OR DIS	OLVED F SIGNIFI SABILITY CAPACITY	CANT OR	SISTE T	NT	
		oort (Post Authorization P) for protocol B18710		udy) rec	eived from c	contac	table			_	""`] LIF		•			
				-	nued on Addit		nforma	tion P	age)	<u> </u>	」	REATENI	NG			
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	CT DRUG	i(S) IN	FORMATI	ION				20.1	DID RE	ACTION				
	TINIB) Film-coated	tablet										AFTER S		PING		
15. DAILY DOSE(S) #1) 500 mg, 1x/da	у			ROUTE(S)) Unkno	OF ADMINISTRA OWN	ATION					YE	S N	o [X N	A	
17. INDICATION(S) FOR #1) Unknown	USE									21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(fro #1) 10-JAN-2019 /	·				DURATION ths 2 days						YE	S N	o [X N	A	
		III. CONCOMI	TANT DR	RUG(S) AND HIS	STOF	RY									_
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those up	sed to treat reac	tion)												
				7												
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23. OTHER RELEVANT H	HISTORY, (e.g. diagnostics.	allergies, pregnancy with last m	onth of period, e	itc.)												\dashv
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med Hi	D	escription	myeloid leuk	emia	(Chro	nic m	yelo	id le	ukae	mia)				
			·		•				•			ŕ				
24a. NAME AND ADDRES	SS OF MANUFACTURER	IV. MANUF	FACTURE	ER INI		ON										\neg
Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva	ard East 01 UNITED STATES	8														
	24b. MFR CC	NTROL NO.			ME AND ADDRES											\dashv
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24c. DATE RECEIVED BY MANUFACTURE 18-JUL-2023		LITERATURE		NAME	E AND ADDRI	ess V	viiHH	ĿLD.								
DATE OF THIS REPORT	PROFES 25a. REPOR															
28-FEB-2024	⊠ INITIAL	FOLLOWUP:														

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.



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1. PATIENT INITIALS	1a. COUNTRY	I. REAC	2a, AGE	3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONSI	FT	8-1:	2 C	HEC	CK ALL	_			_
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	36	Female	_	Day	Monti	n ,	Year 017	1	Α	PPR	OPRIA RSE R	ATE T			
Mixed dyslipidaeı	CTION(S) (including relevant RRED TERM] (Related symp mia [Dyslipidaemia] balance [Blood glud		s)							1		NVOL PROL	ENT DIE LVED C LONGEI PITALIS	OR D INI		:NT	
	: OBSERVATIONAL FE CONDITIONS (L STUDY- EVALUATIOI DF USE	N OF EFF	FICACY	AND SAFET	Y OF	BOSL	JLIF		ן נ	– 0	OR SI DISAE	LVED P IGNIFIC BILITY	CANT OR		NT	
		oort (Post Authorization P) for protocol B187104		tudy) rec	eived from co	ontac	table						PACITY	ſ			
				(Conti	nued on Addit	ional lı	nforma	tion P	age)			IFE HRE	ATENII	NG			
		II. SUSPEC	T DRUC	G(S) IN	FORMATI	ON											
14. SUSPECT DRUG(S) #1) Bosulif (BOSU #2) NILOTINIB (N	JTINIB) Film-coated	tablet		(Conti	nued on Additi	ional lı	nforma	ition P	age)		DID R ABAT DRUC	EAF	TION TER S	STOP	PPING		
15. DAILY DOSE(S) #1) 100 mg, daily #2) UNK			#	s. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRATION	TION					Ч	/ES	□ NO	o [X N/	Α	
17. INDICATION(S) FOR #1) Unknown #2) Chronic myelo	use ogenous leukemia (C	a)							21.		PPEA	CTION AR AFT DUCTI		,			
18. THERAPY DATES(fro #1) 18-APR-2016 #2) 01-JUL-2017	/ 01-MAY-2016		#-	o. THERAPY 1) 14 day 2) Unkno	S						ПΥ	/ES	□ NO	0 [X N	A	
		III. CONCOMIT	ANT DI	RUG(S	AND HIS	STOF	RΥ										
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	IINISTRATION (exclude those use	ed to treat rea	action)													
22 OTHER RELEVANT	LUCTORY (a.g. diagnostics	allergies, pregnancy with last mor	nth of nariad	oto \													
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med His		Description	nyelogenous	s leuk	emia	(Chro	nic	mve	loid	leu'	kaem	nia)			
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O45 NAME AND ADDDE	SS OF MANUFACTURER	IV. MANUF	ACTUR	ER INF		NC						_					
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07-SEP-2023	HEALTH	SSIONAL OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:															

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 Lah Data					
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# Date	Test / Assess	sment / Notes	Results	Normal High / Low
1	Blood glud	cose	imbalance	
14-19. SUSPECT DRUG(S) con	tinued			
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) Fil	m-coated tablet;	200 mg, daily; Unknown	Unknown	02-MAY-2016 /
Regimen #2				15-MAY-2016;
				14 days
#1) Bosulif (BOSUTINIB) Fil	m-coated tablet;	300 mg, daily; Unknown	Unknown	16-MAY-2016 /
Regimen #3				20-APR-2017;
				11 months 5 days
#1) Bosulif (BOSUTINIB) Fil	m-coated tablet;	400 mg, daily; Unknown	Unknown	21-APR-2017 /
Regimen #4		•		30-JUN-2017;
				2 months 10 days

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SHEDEC	T ADVEDSE I	REACTION REPO	DT															
SUSPEC	I ADVERSE I	REACTION REPO	KI										_					
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1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION I	NFOR 3. SEX	MATION 3a. WEIGHT		REACTION C	NISET	8-12	CHECK	· ALI							
(first, last)	FRANCE	Day Month Year	1 ₆₇		Unk	Day Day	Month	Year	1 .	APPRO ADVER	PRIATE		٨					
PRIVACY	Teas to the second seco																	
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)										PATIEN	T DIEC							
Diarrhea grade 1 Fall (having cause		Falli							INVOLVED OR PROLONGED INPATIENT									
, ,	, -	rade 1 [Contusion]								HOSPI	TALISA"	ΓΙΟΝ						
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE								╵╙╵	INVOLV OR SIG DISABI INCAPA	NIFICA LITY OI	.NT	ENT						
This is a non-inter	ventional study re	port (Post Authorizatior	n Safety St	udy) rec	eived from	contac	table											
reporter(s) (Physic	cian and Other HC	P)		(Conti	nued on Add	ditional I	nformatio	n Page)		LIFE THREA	TENIN	3						
							mormatio	ni i age,		THINEA	LIVIIV							
14 SUSPECT DRUG(S)	include generic name)	II. SUSPEC	T DRUG	S(S) IN	FORMA	TION			20. DID	REACT	ION							
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet										TE AFT		OPPING	3					
15. DAILY DOSE(S)			16	POLITE(S)	OF ADMINISTI	PATION			ł									
					wn			YES [NO	M	IA							
17. INDICATION(S) FOR USE #1) Unknown									21. DID REA	REACT APPEAR NTROD	R AFTE	3						
,						REII	NIROD	UCTIO	N?									
18. THERAPY DATES(from #1) 14-SEP-2017 /	. THERAPY I) Unkno					0	YES [NO	NO NA									
		III. CONCOMI	TANT DE	RUG(S	AND H	ISTO	RY											
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat read	ction)														
23. OTHER RELEVANT H	IISTORY. (e.g. diagnostics	, allergies, pregnancy with last me	onth of period,	etc.)														
From/To Dates Unknown		Type of History / Notes	[Description														
		IV/ MANITE	ACTUR	EB INI	ORMAT	ION												
IV. MANUFACTURER I 24a. NAME AND ADDRESS OF MANUFACTURER 26. 1						ION												
Pfizer Inc Stella Pietrafesa																		
66 Hudson Bouleva New York, NY 1000	1 UNITED STATE	S																
Phone: 212 733 40	45	7																
	24b. MFR CO	ONTROL NO.		25b. NAME AND ADDRESS OF REPORTER														
	PV20230	00127226		NAME	AND ADD	RESS V	VITHHEL	.D.										
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR			NAME	AND ADD	RESS V	VITHHEL	.D.										
20-JUL-2023	STUDY																	
DATE OF THIS REPORT	25a. REPOR			1														
28-FEB-2024	⊠ INITIAL	FOLLOWUP:																

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.

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SUSPEC	T ADVERSE F	REACTION REPO	RT																	
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													\perp							
		I. REA	CTION	INFOR	MATION		7													
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT			ON ONS		8-1			CK ALL		то					
PRIVACY FRANCE Day Month PRIVACY Unk Female Unk Day Month AUG 202													ERSE I			N				
7 + 13 DESCRIBE REACTI Event Verbatim [PREFERR Other Serious Crite Miscarriage [Aborti	PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION																			
Case Description: OBSERVATIONAL STUDY - EVALUATION OF EFFICACY AND SAFETY OF BOSULIF UNDER REAL-LIFE CONDITIONS OF USE							[OR S	OLVED SIGNIFI BILITY	ICAN Y OR	١T	ENT							
This is a non-interventional study report received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.									INCAPACITY											
				(Conti	nued on Additio	nal Ir	nforma	ation F	age	*) L		IFE HRE	EATEN	IING						
		II. SUSPEC	T DRU	G(S) IN	FORMATIC	N														
14. SUSPECT DRUG(S) (in #1) Bosulif (BOSUT	-	tablet						,		20.	DID R ABAT DRUC	ГΕΑ	CTION FTER		PPING	PING				
15. DAILY DOSE(S) #1) 500 mg, daily					. ROUTE(S) OF ADMINISTRATION 1) Unknown								YES NO NA							
17. INDICATION(S) FOR U: #1) Unknown	SE									21.		PPE	CTION AR AF DDUCT	TER						
18. THERAPY DATES(from #1) 21-MAR-2019 /				9. THERAPY †1) 1 year							П	ſES _		10	⊠ Ւ	NA				
		III. CONCOMIT	TANT D	RUG(S) AND HIS	ΓOR	Υ													
	1.1	MINISTRATION (exclude those use			<u>, - </u>		<u>-</u>													
#1) DASATIND (D	ASAIINID, , 51-	-MAR-2020 / Ongoing																		
23. OTHER RELEVANT HIS	STORY. (e.g. diagnostics,	, allergies, pregnancy with last mo Type of History / Notes		, etc.) Description																
Unknown		туре отпоску / посс			.MP for pregna	ancy														
	,	D/ MANUE				N I														
IV. MANUFACTURE 24a. NAME AND ADDRESS OF MANUFACTURER					-ORMATIO 1ARKS	N														
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevar New York, NY 10001 Phone: 212 733 404																				
	24b. MFR CO	INTROL NO.		ı	ME AND ADDRESS															
	PV20230	00129493		NAME AND ADDRESS WITHHELD. NAME AND ADDRESS WITHHELD.																
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	T SOURCE LITERATURE		INAIVIE	ANDADDRE	33 W	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	IELD.												
31-OCT-2023	HEALTH PROFES	SSIONAL OTHER:																		
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																				

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.

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SUSPEC	T ADVERSE F	REACTION REPO	ORT															
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1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION II	NFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONSE	FT	8-12) CH	IECK ALI	_					
(first, last) PRIVACY	FRANCE Day Month Year 33 96 00 Day Month									ear APPROPRIATE TO ADVERSE REACTION								
7 + 13 DESCRIBE REAC Event Verbatim [PREFER Hepatic steatosis Hypertriglycerider	aas)	PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION																
Case Description: UNDER REAL-LII	ON OF EFF	FICACY	AND SAFET	Y OF	BOS	ULIF		[OF DIS	VOLVED R SIGNIF SABILITY	ICAN OR	١T	ENT					
		oort (Post Authorization P) for protocol B18710		udy) red	eived from c	ontac	table			_		CAPACIT	Υ					
				(Cont	inued on Addit	ional I	nforma	tion P	age)) LIFE THREATENING								
		II. SUSPEC	CT DRUG	(S) IN	FORMATI	ON				_								
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet					inued on Addit	age)	20. DID REACTION ABATE AFTER STOPPING DRUG?											
15. DAILY DOSE(S) #1) 200 mg, daily) Unkno	OF ADMINISTRA OWN			YE	ES N	10	×	IA								
17. INDICATION(S) FOR #1) Unknown	USE									1	REAP	EACTION PEAR AF RODUCT	TER	?				
18. THERAPY DATES(fro #1) 12-NOV-2018	·			19. THERAPY DURATION #1) 1 month 15 days YES NO NA										IA				
		III. CONCOMI) AND HIS	TOF	RY											
	1.1	MINISTRATION (exclude those u -MAR-2020 / Ongoing	sed to treat reac	tion)														
				7														
	HSTORY. (e.g. diagnostics,	allergies, pregnancy with last m																
From/To Dates Unknown to Ongo	ping	Type of History / Notes Relevant Med Hi		escription CML (Ch	ronic myeloi	d leuk	aemia	a)										
		1\ /		ייאו סב) NI												
24a. NAME AND ADDRESS OF MANUFACTURER					RER INFORMATION 26. REMARKS													
Pfizer Inc Stella Pietrafesa 66 Hudson Boulev New York, NY 1000 Phone: 212 733 40	1 UNITED STATES	5																
	24b. MFR CC	ONTROL NO.		25b. NA	ME AND ADDRES	S OF R	EPORTE	ER					_					
		00129521			E AND ADDRE													
24c. DATE RECEIVED BY MANUFACTURE	R 24d. REPOR	T SOURCE		NAME	AND ADDRE	ESS V	/ITHH	ELD.										
28-SEP-2023	HEALTH PROFES	ш																
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																		

Normal High / Low

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.

Test / Assessment / Notes

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.	Lat) D	a	ta	
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Date

11 Date 1001/1100	occinione, motor	rtoodito	rtomarriigir/ Low
1 Ultraso	und 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 table	t; 300 mg, daily; Unknown	Unknown	27-DEC-2018 /
Regimen #2			14-JAN-2019;
			19 days
#1) Bosulif (BOSUTINIB) Film-coated table	t; 400 mg, daily; Unknown	Unknown	15-JAN-2019 /
Regimen #3			20-MAR-2019;
			2 months 6 days
#1) Bosulif (BOSUTINIB) Film-coated table	t; 500 mg, daily; Unknown	Unknown	21-MAR-2019 /
Regimen #4			30-MAR-2020;
			1 year 10 days

Results

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SUSPECT A	DVERSE R	EACTION REPO	RT									_		_			
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							\square				\perp		\perp	\perp			
		I. REAC	CTION I	INFOR	MATION												
(first, last)	a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE 35	3. SEX		4-6 RI	ACTIO	N ONSI	ET Year	8-1:	,	APPF	CK ALL	ATE			
PRIVACY ''	VANOL	PRIVACY	Years	Male		Ó	SEF	2	02	1	,	ADVI	ERSE F	₹EA(CHO	N	
7 + 13 DESCRIBE REACTION(S) Event Verbatim [PREFERRED TE Hepatic cytolysis [Hepa	RM] (Related symp	tests/lab data) toms if any separated by commas	s)							l E		INVO	ENT DI	OR			
Case Description: OBS UNDER REAL-LIFE CO			N OF EF	FICACY	AND SAFETY	′ OF	BOS	ULIF				HOS	LONGE PITALIS	SATI	ION		
This is a non-intervention reporter(s) (Physician a				tudy) rec	eived from co	ntact	able					OR S	SIGNIFI ABILITY APACIT	ICAN 'OR	١T	INI	
				(Conti	nued on Additio	nal Ir	ıforma	ition P	age	, [LIFE THRE	EATEN	IING			
		II. SUSPEC	T DRUC	3(S) IN	FORMATIO	N				<u> </u>							
14. SUSPECT DRUG(S) (include #1) Bosulif (BOSUTINIB #2) DASATINIB (DASAT) Film-coated t		1 DIXOC	<u> </u>	TOTAL TITLE					20.		TE A	CTION FTER S		PPING	3	
15. DAILY DOSE(S) #1) 500 mg #2) UNK	iivib)		#1	1) Oral	OF ADMINISTRATI	ON						YES	. □N	Ю	⊠⊦	IA	
17. INDICATION(S) FOR USE #1) Unknown	CATION(S) FOR USE 21. DID REACTION PEADDEAD AFTER																
18. THERAPY DATES(from/to) #1) 21-MAR-2019 / 30-N #2) 31-MAR-2020 / Ong	/AR-2020	Thyelold leukaethia)	#1	. THERAPY 1) 1 year 2) Unkno	10 days							YES	N	Ю	⊠⊦	ΙA	
		III. CONCOMIT	ANT DE	RUG(S) AND HIST	ΓOR	Υ										
22. CONCOMITANT DRUG(S) AN	ID DATES OF ADM	INISTRATION (exclude those use	ed to treat rea	ction)													
23. OTHER RELEVANT HISTORY From/To Dates	Y. (e.g. diagnostics,	allergies, pregnancy with last mor		etc.) Description													
Unknown to Ongoing																	
		1\/ \/ \/ \\	A CTLID	ED IVI		N.I											
24a. NAME AND ADDRESS OF M	MANUFACTURER	IV. MANUF	ACTUR	26. REM		IN											
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard Ea New York, NY 10001 UN Phone: 212 733 4045																	
	24b. MFR COI	NTROL NO.		25b. NA	ME AND ADDRESS	OF RI	PORTI	ΞR									
	PV20230	0129527			AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE LITERATURE		NAME	AND ADDRES	SS W	/ITHH	ELD.									
28-SEP-2023	M HEALTH PROFES	ш															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:															

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.

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SUSPEC	CT ADVERSE F	REACTION REPO	RT														
		I. REA	CTION II	NFORM	MATION				1		<u> </u>						_
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE		3a. WEIGHT	4-6 RE	ACTIO	N ONS	ET Year	8-1:	AF	HECK A	RIATI				_
PRIVACY	FRANCE	PRIVACY	69 Years	emale	52.00 b	ay	API		2019	9	ΑD	OVERSI	E RE	ACTIC	N		
Event Verbatim [PREFER	TION(S) (including relevant RED TERM] (Related sympy ynia [Glossodynia]	otoms if any separated by comma	as)]		VOLVE	D OF	₹	TENT	T	
•	: OBSERVATIONA FE CONDITIONS (L STUDY - EVALUATIO OF USE	ON OF EFF	FICACY A	ND SAFETY	OF	BOS	ULIF			НС	VOLVE	LISA	TION			
		oort (Post Authorization P) for protocol B18710	•	udy) rece	ived from cor	ntact	able				OF DI:	R SIGN SABILI CAPAC	IIFICA TY O	TNA			
				(Contin	ued on Additio	nal In	ıforma	ation F	age	, [FE HREATE	ENIN	G			
		II. SUSPEC	T DRUG	(S) INF	ORMATIC)N											
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name) ITINIB) Film-coated	tablet						,		20.	DID RE ABATE DRUG	AFTE		OPPIN	IG		
15. DAILY DOSE(S) #1) 300/200 mg al	ternately, daily			ROUTE(S) O) Unknow	OF ADMINISTRATION	ON					YE	ES [] NO	×	NA		
17. INDICATION(S) FOR #1) Unknown										21.		EACTIC PEAR A RODU	AFTE				
18. THERAPY DATES(fro #1) 26-FEB-2018	•			THERAPY D							YE	ES] NO		NA		
	III. CONCOMITANT DRUG(S) AND HISTORY																
22. CONCOMITANT DRU	ONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)																
	OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) //To Dates Description																
Unknown to Ongo	ping	Relevant Med His			yeloid leuker	mia (Chro	nic m	nyelo	oid le	ukae	mia)					
		IV. MANUF	ACTURE	ER INF	ORMATIO	N											-
24a. NAME AND ADDRE	SS OF MANUFACTURER			26. REMA													
Stella Pietrafesa 66 Hudson Boulev New York, NY 1000 Phone: 212 733 40	1 UNITED STATES	3															
	24b. MFR CC	ONTROL NO.		25b. NAM	E AND ADDRESS	OF RF	PORT	ER									_
		00129529			AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR	T SOURCE LITERATURE		NAME A	AND ADDRES	SS W	'ITHH	IELD.									
27-SEP-2023	M HEALTH PROFES	ш															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE FOLLOWUP:															

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.

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		I DEA	CTION I	NEOD	MATION	<u> </u>								
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	_	REACTION	ONSET	8-12		ECK ALL			
(first, last) PRIVACY	FRANCE	Day PRIVACY Year	34 Years	Male	96.00 kg	Day 14	Month SEP	Year 202			PROPRIA VERSE F		NC	
		tests/lab data) otoms if any separated by comma norphology abnormal]	as)						2	J J INV	OLVED (OR	TIEN'	т
Case Description: 0		L STUDY - EVALUATIO OF USE	ON OF EFF	FICACY	AND SAF	ETY O	F BOSL	JLIF		HO	SPITALIS	SATION		
This is a non-interv protocol B1871047	, ,	port received from conta	actable rep	oorter(s)	(Physicia	n and C	Other H	CP) for		OR DIS	SIGNIFI ABILITY APACIT	CANT OR	ILINI	
A 34-year-old male	patient received	bosutinib (BOSULIF), f	rom	(Conti	nued on Ad	ditional	Informat	ion Page	e)] LIFI	E REATEN	ING		
		II. SUSPEC	T DRUG	S(S) IN	FORMA	TION								
14. SUSPECT DRUG(S) (in #1) Bosulif (BOSUT #2) DASATINIB (DA	INIB) Film-coated	tablet		` '					1 /		ACTION AFTER S		NG	
15. DAILY DOSE(S) #1) 500 mg, daily #2) UNK			#1	ROUTE(S)) Unkno) Oral	OF ADMINIST WN	RATION			ا	YE	s 🔲 N	.0 🛛	NA	
	Unknown Chronic myeloid leukemia (Chronic myeloid leukaemia) REAPPEAR AFTER REINTRODUCTION?													
· '														
	III. CONCOMITANT DRUG(S) AND HISTORY													
22. CONCOMITANT DRUG	CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)													
	3. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)													
From/To Dates Unknown to Ongoin	om/To Dates Type of History / Notes Description Inknown to Ongoing Relevant Med History Chronic myeloid leukemia (Chronic myeloid leukaemia)													
		IV. MANUF	ACTURI	ER INF	ORMA	ΓΙΟΝ								
24a. NAME AND ADDRESS Pfizer Inc	S OF MANUFACTURER			26. REN										
Stella Pietrafesa 66 Hudson Boulevar New York, NY 1000 Phone: 212 733 404	I UNITED STATES	3												
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28-SEP-2023	STUDY HEALTH PROFES	LITERATURE SSIONAL OTHER:												
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT													

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.



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SUSPECT	ΓADVERSE F	REACTION REPO	RT														
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		I. REAC	CTION II	NFOR	MATION												
PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE	3. SEX	_	4-6 RI	EACTIO Month	_	ET Year	┥.		APP	CK ALL ROPRIA	TE T			
PRIVACY	TRANCE	PRIVACY	Years	Male		2	MAF	₹ 2	202	0		ADVI	ERSE R	EAC	HON		
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERRE hepatic cytolysis [Ho	ED TERM] (Related symp	tests/lab data) otoms if any separated by commas	s)									INVO	ENT DIE	OR			
Case Description: C UNDER REAL-LIFE		L STUDY- EVALUATION OF USE	N OF EFF	ICACY A	AND SAFETY	OF I	BOSL	JLIF				HOS	LONGEI PITALIS DLVED P	SATIO	N		
		oort (Post Authorization P) for protocol B187104		udy) rec	eived from co	ntact	able				ш	OR S	SIGNIFIC ABILITY (APACITY	CANT OR			
				(Conti	nued on Additio	nal Ir	nforma	ition F	Page	<u>,</u>		LIFE THRI	EATENII	NG			
		II. SUSPEC	T DRUG	(S) IN	FORMATIC	DN											
14. SUSPECT DRUG(S) (inc #1) Bosulif (BOSUTI #2) SPRYCEL (DAS	INIB) Film-coated	tablet		<u> </u>						20	AB/		CTION AFTER S	TOP	PING		
15. DAILY DOSE(S) #1) 500 mg, daily #2) UNK			#1	ROUTE(S)) Unkno) Oral	OF ADMINISTRATI WN	ON						YES	s 🔲 NC	> [N/	۸	
17. INDICATION(S) FOR US #1) Unknown #2) CML (Chronic m	Unknown CML (Chronic myeloid leukaemia)																
· ·	19. THERAPY DATES(from/to) 19. THERAPY DURATION #1) 1 year 10 days 131-MAR-2020 / Ongoing 19. THERAPY DURATION #2) Unknown																
		III. CONCOMIT	ANT DR	UG(S) AND HIST	ГOR	Υ										
22. CONCOMITANT DRUG(2. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)																
From/To Dates		allergies, pregnancy with last mor Type of History / Notes	D	escription				,									
Unknown to Ongoin	Unknown to Ongoing Relevant Med History CML (Chronic myeloid leukaemia)																
		IV. MANUF	ACTURI	ER INF	ORMATIO	N											
24a. NAME AND ADDRESS Pfizer Inc	OF MANUFACTURER	12.100.0.1017		26. REM													
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES	3															
	Louis Medica	INITROL NO		OFF NO	ME AND ADDRESS	05.5	-DOCT	-D									
	24b. MFR CC PV20230	00129596			ME AND ADDRESS AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT			NAME	AND ADDRES	SS W	/ITHH	ELD.									
28-SEP-2023	STUDY HEALTH PROFES	SSIONAL DITERATURE															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT																

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.

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SUSPECT A	DVERSE REACTION REPOR	RT		
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	I RΕΔ(CTION IN	NFORMATION	
	a. COUNTRY 2. DATE OF BIRTH	1 1	3. SEX 3a. WEIGHT 4-6 REACTION ONSET	8-12 CHECK ALL
PRIVACY	RANCE Day Month PRIVACY Year	47 Years F	emale 59.50 Day Month Year 2020	APPROPRIATE TO ADVERSE REACTION
) (including relevant tests/lab data) ERM] (Related symptoms if any separated by commas Inctional gastrointestinal disorder]	as)		PATIENT DIED INVOLVED OR
Case Description: OBS UNDER REAL-LIFE CO	SERVATIONAL STUDY - EVALUATIO ONDITIONS OF USE	ON OF EFF	FICACY AND SAFETY OF BOSULIF	PROLONGED INPATIENT HOSPITALISATION
	onal study report (Post Authorization for protocol B1871047.	n Safety Stu	udy) received from contactable	INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
			(Continued on Additional Information Page)	LIFE THREATENING
	II. SUSPEC	T DRUG	(S) INFORMATION	
14. SUSPECT DRUG(S) (include #1) Bosulif (BOSUTINIE	-			20. DID REACTION ABATE AFTER STOPPING DRUG?
15. DAILY DOSE(S) #1) 500 mg, daily			ROUTE(S) OF ADMINISTRATION) Unknown	YES NO NA
17. INDICATION(S) FOR USE #1) Unknown				21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
18. THERAPY DATES(from/to) #1) MAR-2020 / Ongoin	g		THERAPY DURATION) Unknown	YES NO NA
	III. CONCOMIT	TANT DR	UG(S) AND HISTORY	
22. CONCOMITANT DRUG(S) AI	ND DATES OF ADMINISTRATION (exclude those use	sed to treat react	ion)	
			_	
	Y. (e.g. diagnostics, allergies, pregnancy with last mor			
From/To Dates Unknown to Ongoing	Type of History / Notes Relevant Med His		escription SML (Chronic myeloid leukaemia)	
	IV. MANUF	 ACTURE	ER INFORMATION	
24a. NAME AND ADDRESS OF I			26. REMARKS	
Stella Pietrafesa 66 Hudson Boulevard Ea New York, NY 10001 UN Phone: 212 733 4045				
	24b. MFR CONTROL NO.		25b. NAME AND ADDRESS OF REPORTER	
	PV202300130373		NAME AND ADDRESS WITHHELD.	
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE		NAME AND ADDRESS WITHHELD.	
12-OCT-2023	STUDY LITERATURE HEALTH PROFESSIONAL OTHER:			
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TYPE INITIAL FOLLOWUP:			

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.

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SUSPEC	T ADVERSE F	REACTION REPO	RT																								
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			CTION II							_																	
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	68 Years	3. SEX Male	3a. WEIGHT	4-6 R Day 27	Mont DE	h	Year 2017		Α	APPR	CK ALL ROPRIA ERSE R	ATE T													
	S AND HEAD [Prur	tests/lab data) toms if any separated by comma 'itus]	as)							1		NVOI PROL	ENT DIE LVED C LONGE PITALIS	OR ED INF		:NT											
UNDER REAL-LII	FE CONDITIONS (ULIF		ן (OR SI	LVED P IGNIFIO BILITY (PACITY	CANT OR	ISTE	NT											
		oort (Post Authorization P) for protocol B18710								,	- .	JFE															
					nued on Addit		nforma	ation P	Page)	<u> </u>	HRE	ATENII	NG													
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	T DRUG	i(S) IN	FORMATI	ON				20.	DID R																
	TINIB) Film-coated	tablet						,			ABAT DRU		FTER S	STOP	PING	i											
15. DAILY DOSE(S) #1) 300 mg, daily) Unkno	OF ADMINISTRA	TION						YES	NO	○ [N/	Α											
17. INDICATION(S) FOR #1) Unknown												PPE/	CTION AR AFT DUCTI														
18. THERAPY DATES(fro #1) 02-MAY-2017	Y DATES(from/to) AY-2017 / 19-MAY-2017 19. THERAPY DURATION #1) 18 days											YES	N	o [N/	A											
		III. CONCOMI	TANT DR	RUG(S) AND HIS	STOF	RY																				
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	INISTRATION (exclude those us	sed to treat reac	tion)																							
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DATE OF THIS REPORT 28-FEB-2024																	F THIS REPORT 25a. REPORT TYPE										

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.



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SUSPECT	ADVERSE R	REACTION REPOR	RT										
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1. PATIENT INITIALS	1a. COUNTRY	1. REAC		3. SEX	MATION 3a. WEIGHT	4-6 RF/	ACTION ON	NSFT	8-12	CHEC	K Al I		
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	71	emale	64.00	Day	Month SEP	Year 2019	1	APPR	OPRIAT	E TO ACTION	I
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERREI Tremor of hands [Tre		tests/lab data) toms if any separated by commas	3)							INVOI	NT DIE	₹	
Case Description: O UNDER REAL-LIFE		STUDY- EVALUATION OF USE	N OF EFF	CACY	ND SAFETY	Y OF B	OSULIF	F		HOSF	PITALISA	INPATIE TION ERSISTE	
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				(Conti	nued on Additi	ional Inf	ormation	n Page)		LIFE THRE	ATENIN	G	
		II. SUSPECT	T DRUG	(S) IN	FORMATI	ON							
14. SUSPECT DRUG(S) (incl #1) Bosulif (BOSUTII	-	rablet							AE	D REAC BATE AF RUG?		OPPING	;
15. DAILY DOSE(S) #1) 300 mg, daily				ROUTE(S)) Oral	OF ADMINISTRAT	TION				YES	NO	×Ν	A
17. INDICATION(S) FOR USI #1) Unknown	E								RE		TION AR AFTE DUCTIO		
18. THERAPY DATES(from/te #1) 05-SEP-2018 / 13	·				DURATION h 8 days					YES	NO	×Ν	A
		III. CONCOMITA	ANT DR	UG(S	AND HIS	TOR	ſ		•				
22. CONCOMITANT DRUG(S	S) AND DATES OF ADM	INISTRATION (exclude those use	ed to treat reac	tion)									
				7									
23 OTHER RELEVANT HIST	TORY (e.g. diagnostics	allergies, pregnancy with last mon	oth of period e	to)									
From/To Dates Unknown	TOR f. (e.g. diagnostics,	Type of History / Notes		escription									
		IV. MANUFA	ACTURE			ON							
24a. NAME AND ADDRESS OF Prizer Inc	OF MANUFACTURER			26. REM	ARKS								
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001													
Phone: 212 733 4045		,											
	24b. MFR CO	NTROL NO.		25b. NA	ME AND ADDRES	S OF REF	PORTER						
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24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		NAME	AND ADDRE	ESS WI	THHELD	D.					
03-OCT-2023	M HEALTH PROFES	ш											
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:											

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.

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		I. REA	CTION	INFOR	MATION									
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PRIVACY	FRANCE	Day Month Year PRIVACY	71 Years	Female	64.00 kg	Day 05	Month JUN	Year 2019			ERSE RI		N	
7 + 13 DESCRIBE REACTI	ION(S) (including relevan	t tests/lab data) ptoms if any separated by comm	<u> </u>		9				_					
Event Verbatim [PREFERR Asthenia [Asthenia		ptoms if any separated by comm	as)								ENT DIE			
depressive syndroi									19	PRO	LVED O LONGEI PITALIS	INPAT	ENT	
Case Description:	OBSERVATIONA	L STUDY - EVALUATION	ON OF EF	FICACY	AND SAFE	ETY OF	BOSUL	.IF		1100	TIVE O	WION		
UNDER REAL-LIF										INVC OR S	LVED P	ERSIST	ENT	
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		P) for protocol B18710					,							
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14. SUSPECT DRUG(S) (ir #1) Bosulif (BOSUT		tablet							A	ID REAG BATE A RUG?	CTION FTER S	TOPPIN	G	
]					
15. DAILY DOSE(S) #1) 300 mg, daily				6. ROUTE(S) 1) Oral	OF ADMINISTE	RATION			1 [YES	□ NC		۱A	
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17. INDICATION(S) FOR U #1) Unknown	ISE								R		CTION AR AFTI DDUCTIO			
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18. THERAPY DATES(from #1) 05-SEP-2018 /	·			9. THERAPY 1)1 mon					[YES			۱A	
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		III. CONCOMI	TANT D	RUG(S) AND HI	ISTOF	RY							
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	MINISTRATION (exclude those us			<i>, , ,</i> , , , , , , , , , , , , , , , ,		• •							
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23. OTHER RELEVANT HIS From/To Dates	STORY. (e.g. diagnostics	, allergies, pregnancy with last m Type of History / Notes		etc.) Description										
Unknown		Type of filstory / Notes		Description										
		IV/ NAVNI IT		ED IVI		ION								
24a. NAME AND ADDRESS	S OF MANUFACTURER	IV. MANUF	ACTUR	26. REM		ION								
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66 Hudson Bouleval New York, NY 1000		S												
Phone: 212 733 404		7												
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03-OCT-2023	HEALTH PROFES	_												
DATE OF THIS REPORT	25a. REPOR			7										
28-FEB-2024	⊠ INITIAL	FOLLOWUP:												

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.

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SUSPEC	T ADVERSE F	REACTION REPO	RT													
		I. REA	CTION II	NFORI	MATION											
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day Month Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 R	EACTIO	ON ONS	ET Year	8-12	APF	ECK ALL PROPRIA	ATE TO			
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				(Conti	nued on Addi	tional I	nforma	ation P	age)] LIFI	E REATENI	iNG			
		II. SUSPEC	T DRUG	(S) INI	FORMAT	ION										_
14. SUSPECT DRUG(S) (#1) Bosulif (BOSU	include generic name) TINIB) Film-coated							,		A		ACTION AFTER S	STOPF	PING		
15. DAILY DOSE(S) #1) 300 mg, daily				ROUTE(S)) Oral	OF ADMINISTRA	ATION				l	YE	S N	∘ ∑	NA		
17. INDICATION(S) FOR #1) Unknown	nown REAPPEAR AFTER REINTRODUCTION?															
18. THERAPY DATES(fro #1) 14-OCT-2019	Y DATES(from/to) 19. THERAPY DURATION #1) 1 year 10 months 13 days ☐ YES ☐ NO ☒ NA										ı					
		III. CONCOMI	TANT DR	UG(S)	AND HIS	STOF	RY									
	NCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction) BOSULIF (BOSUTINIB); 03-DEC-2021 / Ongoing															
23. OTHER RELEVANT F	THER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) Type of History / Notes Description															
Unknown		Relevant Med His			bladder (Ca	alculus	blad	der)								
		IV. MANUF	ACTUR			ON										
24a. NAME AND ADDRES Pfizer Inc Stella Pietrafesa	SS OF MANUFACTURER			26. REM	ARKS											
66 Hudson Bouleva	1 UNITED STATES	3														
	24b. MFR CC PV20230	00158539			AND ADDRE											
24c. DATE RECEIVED BY MANUFACTURE	R 24d. REPORT	T SOURCE		NAME	AND ADDR	ESS V	VITHH	IELD.								
05-OCT-2023	M HEALTH PROFES	ш														
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE														

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 suspect 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.

1	3	l ah	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	strictly normal	

Without pleural effusion

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		I. REA	CTION II	NFOR	MATION												
1. PATIENT INITIALS (first, last) PRIVACY	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year PRIVACY	2a. AGE 68 Years	3. SEX Male	3a. WEIGHT 84.00 kg	4-6 R Day 07	Mon	th	Year			APP	CK ALL ROPRIA ERSE R				
ostial stenosis of t	RED TERM] (Related sym _i :he right renal arte।	otoms if any separated by comm ry [Renal artery stenos	sis]	tract co	ingestion]					1		INVO PROI	ENT DIE DLVED C LONGEI PITALIS	OR D INP		NT	
			ON OF EFF	FICACY	AND SAFET	TY OF	BOS	SULIF	:	1	ш	OR S	OLVED P SIGNIFIC BILITY	CANT OR	STEI	NT	
			n Safety St	udy) rec	eived from c	ontac	table						PACITY	,			
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		II. SUSPEC	CT DRUG	(S) IN	FORMAT	ON											
	(Continued on Additional Information Paul II. SUSPECT DRUG(S) INFORMATION ISPECT DRUG(S) (include generic name) Bosutinib (BOSUTINIB) Unknown ILY DOSE(S) 300 mg, daily DICATION(S) FOR USE													TOPF	PING		
15. DAILY DOSE(S) #1) 300 mg, daily	III. SUSPECT DRUG(S) (include generic name) (southint) For USE (S) (Physician and Other HCP) III. SUSPECT DRUG(S) (include generic name) (southint) For USE (include generic name) (southint) (sout													▷	∑ NA	l.	
17. INDICATION(S) FOR #1) Unknown	USE									21.	RE/	APPE.	CTION AR AFT DDUCTI				
18. THERAPY DATES(fro #1) 02-MAY-2017	·											YES	N	▷	∑ NA	l.	
) AND HIS	STOF	RY										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat read	tion)													
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22 OTHER RELEVANT L	JISTORY (o.g. diagnostics	allergies prognancy with last m	anth of pariod a	to \													
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		IV. MANUF	FACTURI	ER INF	ORMATI	NC											
Pfizer Inc Stella Pietrafesa 66 Hudson Bouleva New York, NY 1000	24a. NAME AND ADDRESS OF MANUFACTURER 26. REMARKS																
	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDRES	SS OF F	REPORT	ER									
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24c. DATE RECEIVED BY MANUFACTURE 03-OCT-2023	R 24d. REPOR' STUDY HEALTH PROFES	LITERATURE		NAME	AND ADDR	ESS V	VITHE	HELD.									
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR			1													

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 hosutinib

The follow-up information received does not alter the previous company clinical evaluation.



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	Continued on Additional Information Page PRIVACY Sear PRIVACY PRIV						
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15. DAILY DOSE(S) #1) 300 mg, daily						ON	YES NO NA
17. INDICATION(S) FOR USE #1) Unknown							REAPPEAR AFTER
PRIVACY FRANCE Day March Vas Sex S							
		III. CONCOMIT	TANT C	RUG(S) AND HIST	ORY	
22. CONCOMITANT DRUG(S) AND DATES OF ADM	INISTRATION (exclude those use	ed to treat re	eaction)			
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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	

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1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT			_		┥.			CK ALL ROPRIA		О		
PRIVACY	FRANCE	PRIVACY	Years	Male	76.30 kg	04						ADV	ERSE R	!EAC	TION		
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			ON OF EFF	ICACY A	AND SAFET	ΓY OF	BOS	ULIF			ш	OR S DISA	OLVED F	CANT OR	SISTE	NT	
This is a non-inter B1871047.	ventional study rep	oort received from con	tactable rep	oorter(s)	(Physician)) for p	rotoco	ol				INCA	PACITY	1			
				(Cont	nued on Addi	itional	Inform	ation l	Page	e)		LIFE THRE	EATENI	NG			
		II. SUSPEC	CT DRUG	S(S) IN	FORMAT	ION											
#1) Bosulif (BOSU	TINIB) Film-coated	tablet						·		20	ABA		CTION FTER S	STOP	PING		
15. DAILY DOSE(S) #1) 300 mg, daily #2) UNK	II. SUSPECT DRUG(S) (including relevant tested and any private programs) all carotid stenosis (Carotid artery stenosis) idemia (Dyslipidaemia) Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF (in Real-Life Condition) interventional study report received from contactable reporter(s) (Physician) for protocol 1047. (Continued on Additional Information Page II. SUSPECT DRUG(S) INFORMATION FER REAL-LIFE CONDITIONS OF USE as a non-interventional study report received from contactable reporter(s) (Physician) for protocol 1047. (Continued on Additional Information Page III. SUSPECT DRUG(S) INFORMATION PECT DRUG(S) (include generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) Sulfi (BOSUTINIS) For USE III. SUSPECT DRUG(S) INFORMATION PLOT DRUG(S) (include generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) Sulfi (BOSUTINIS) For USE III. SUSPECT DRUG(S) INFORMATION PLOT DRUG(S) (includes generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) PLOT 2020 (Includes generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) PLOT 2020 (Includes generic name) Sulfi (BOSUTINIS) Film-coated tablet ILLOTINIS (Includes generic name) III. CONCOMITANT DRUG(S) AND HISTORY III. CONCOMITANT DRUG(S)					YES	N	• [N/	Α							
#1) Chronic myelo #2) Chronic myelo	genous leukemia (C genous leukemia (C		nia)							21	REA	APPE.	CTION AR AFT DDUCT				
,	/ 16-JAN-2021		#1) 2 mon	ths 24 days							YES	N	o [N/	A	
		III. CONCOMI	TANT DR	RUG(S) AND HI	STO	RY										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those u	used to treat reac	tion)													
23. OTHER RELEVANT H From/To Dates Unknown to Ongo		Type of History / Notes	D	escription	myelogenou	ıs leul	kemia	(Chro	onic	: mye	eloid	J leu	ıkaen	nia)			
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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.

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	(Continued on Additional Information Page) II. SUSPECT DRUG(S) INFORMATION																					
	SUSPECT DRUG(S) (include generic name)) Bosulif (BOSUTINIB) Film-coated tablet (Continued on Additional Information Page) DAILY DOSE(S) 16. ROUTE(S) OF ADMINISTRATION													20. DID REACTION ABATE AFTER STOPPING DRUG?								
15. DAILY DOSE(S) #1) 200 mg, 1x/da	Bosulif (BOSUTINIB) Film-coated tablet (Continued on Additional Information Page) AILY DOSE(S) 200 mg, 1x/day 16. ROUTE(S) OF ADMINISTRATION #1) Unknown												□N	.0	X N	A						
17. INDICATION(S) FOR #1) Chronic myeld	AILY DOSE(S) 200 mg, 1x/day 16. ROUTE(S) OF ADMINISTRATION #1) Unknown												21. DID REACTION REAPPEAR AFTER REINTRODUCTION?									
18. THERAPY DATES(fro #1) 23-MAY-2016	•			. THERAPY 1)22 day						YES NO NA												
		III. CONCOMIT) AND HIST	OR	Υ															
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	HISTORY. (e.g. diagnostics,	, allergies, pregnancy with last mo	nth of period,	etc.)													_					
From/To Dates Unknown to Ongo	ping	Type of History / Notes Relevant Med His		Description Chronic 1	myeloid leuker	nia (Chro	nic m	nyel	oid le	∍uka	aem	ia)									
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24a. NAME AND ADDRESS OF MANUFACTURER Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																						
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03-OCT-2023	HEALTH PROFES			4																		
28-FEB-2024	25a. REPOR	FOLLOWUP:																				

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;	100 mg, 1x/day; Unknown	Chronic myeloid leukemia	20-JUN-2016 /	
Regimen #2		(Chronic myeloid leukaemia)	26-JUN-2016;	
			7 days	

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17. INDICATION(S) FOR #1) Unknown	USE									21.	REA	APPE	CTION EAR AFT ODUCT	TER	?		
18. THERAPY DATES(fro #1) 06-NOV-2019	·			9. THERAPY 1) 1 year	DURATION 9 months 5 c	days						YES	S N	.0	×Ν	A	
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	JG(S) AND DATES OF ADM MATINIB) ; 21-DEC	IINISTRATION (exclude those us C-2021 / Ongoing	ed to treat re	action)													
23. OTHER RELEVANT From/To Dates	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo	onth of period	, etc.) Description													
Unknown to Ong	oing	Relevant Med His	story		myeloid leuk	aemia	a (Chr	onic	mye	loid	leuk	(aei	mia)				
		IV. MANUF	ACTUF	RER INF	ORMATION	ON											
Pfizer Inc	ESS OF MANUFACTURER			26. REM	IARKS												
Stella Pietrafesa 66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	3															
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03-OCT-2023	HEALTH PROFES			_													
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TTYPE FOLLOWUP:															

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

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1. PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 66	3. SEX	_	4-6 RI	EACTIC	_	SET Yea	┥.	-12	APP	ROPRI	ATE			
PRIVACY	ITANOL	PRIVACY	Years	Male		9	MA	R 2	202	2		ADV	ERSE F	KEA	CHO	N	
	(S) (including relevant TERM] (Related symp	tests/lab data) otoms if any separated by comma	s)									PAT	IENT DI	ED			
dyspnea [Dyspnoea] inappetence [Decreas	sed appetite]											PRC	OLVED DLONGE SPITALIS	ED IN		ENT	
		L STUDY- EVALUATIO	N OF EFI	FICACY	AND SAFETY	OF I	BOSI	JLIF			_	INIV	OLVED	DED	ејет	ENIT	
UNDER REAL-LIFE (Ш	OR DIS	SIGNIFI ABILITY APACIT	ICAN 'OR	ΝT	_1111	
		oort (Post Authorization P) for protocol B18710		tudy) rec	eived from co	ntact	able					INC	APACII	ī			
				(Cont	nued on Additio	nal Ir	nforma	ation I	Page	e)		LIFE	EATEN	IING			
		II. SUSPEC	T DRU	G(S) IN	FORMATIC	NC				- 1				_			
14. SUSPECT DRUG(S) (inclu	-			<u> </u>						20			ACTION AFTER S		PPIN	<u> </u>	
#1) Bosulif (BOSUTIN #2) IMATINIB (IMATIN	,	tablet		(Cont	nued on Additio	nal Ir	nforma	ation I	Page	e)		RUG?					
15. DAILY DOSE(S) #1) 300 mg, daily #2) UNK			#	6. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRATION	ON						YES	S 🔲 N	10	×	IA	
17. INDICATION(S) FOR USE #1) Unknown #2) Chronic myeloid le	eukemia (Chronic	c myeloid leukaemia)								21	RE	APP	ACTION EAR AFT ODUCT	TER			
18. THERAPY DATES(from/to) #1) 06-NOV-2019 / 10 #2) 21-DEC-2021 / Or	-AUG-2021		#	o. THERAPY 1)1 year 2)Unkno	9 months 5 da	ıys						YES	S 🔲 N	10	×	IA	
		III. CONCOMIT	TANT D	RUG(S) AND HIST	ΓOR	RΥ										
22. CONCOMITANT DRUG(S)	AND DATES OF ADM	IINISTRATION (exclude those us	ed to treat rea	action)													
From/To Dates		allergies, pregnancy with last mo Type of History / Notes		Description													
Unknown to Ongoing		Relevant Med His	story	Chronic	myeloid leukei	mia ((Chro	nic m	nyel	loid l	euk	aen	nia)				
	,	IV. MANUF	ACTUR	PER INI		N											
24a. NAME AND ADDRESS O Pfizer Inc	F MANUFACTURER	17.17.17.17.17.17.17.17.17.17.17.17.17.1	7.0101	26. REN													
Stella Pietrafesa 66 Hudson Boulevard	Fast																
New York, NY 10001 I Phone: 212 733 4045		3															
														_			
	24b. MFR CO	NTROL NO. 00165373			ME AND ADDRESS AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		NAME	AND ADDRES	SS W	/ITHH	IELD.									
03-OCT-2023	STUDY HEALTH PROFES	LITERATURE OTHER:															
DATE OF THIS REPORT	25a. REPORT			\dashv													
28-FEB-2024	⊠ INITIAL	FOLLOWUP:															

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

										CIO	OMS	FOF	₹M
SUSPECT	Γ ADVERSE F	REACTION REPO	RT										_
						11		П		П		T	Н
		I. REA	CTION	INFOR	MATION								
1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	3a. WEIGHT	$\overline{}$	TION ONSET	_		HECK ALL			
PRIVACY	FRANCE	Day Month Year PRIVACY	66 Years	Male	67.00 kg			ear 121			REACTIO	N	
7 + 13 DESCRIBE REACTION	ON(S) (including relevant	tests/lab data) toms if any separated by comma	ne)						□ PA	TIENT DI	ED		
asthenia [Asthenia]								T,		VOLVED	OR		
		D AND SCALP [Skin le	-		47					SPITALIS	ED INPATI SATION	ENT	
Case Description: CUNDER REAL-LIFE		L STUDY- EVALUATIO DF USE	N OF EF	FICACY	AND SAFET	Y OF BC	SULIF		☐ IN	VOLVED	PERSISTI	ENT	
This is a non-interv	entional study rer	oort (Post Authorization	Safety S	study) red	reived from c	rontactab	<u>م</u> ا		DI	R SIGNIFI SABILITY CAPACIT	OR		
		P) for protocol B18710		ituuy, roc	elved Holli o	Unacias	iic						
				(Cont	inued on Addit	tional Info	rmation Pa	_{ige)} [E IREATEN	ING		
		II. SUSPEC	T DRU	G(S) IN	IFORMAT	ION							
14. SUSPECT DRUG(S) (inc	-			O (O).				20.		ACTION AFTER S	STOPPIN	G	\neg
#1) Bosulif (BOSUT	INIB) Film-coateu	tablet							DRUG			_	
15. DAILY DOSE(S) #1) 300 mg, 1x/day				6. ROUTE(S 11) Unkno	OF ADMINISTRA	ATION			Y	ES □N	0 🛛	NΑ	
17. INDICATION(S) FOR US	SE			4		7		21.	REAPI	ACTION PEAR AF			
#1) Unknown								_		RODUCT			
18. THERAPY DATES(from/ #1) 06-NOV-2019 / 0	•			9. THERAPY 11) Unkno					Y	ES N	0 🛛	NA 	
		III. CONCOMIT	TANT D	RUG(S) AND HIS	STORY							
22. CONCOMITANT DRUG(IINISTRATION (exclude those us	sed to treat rea	action)									
#2) EZETROL (EZ	ETIMIBE); Ong	oing											
#3) BISOPROLOL	(BISOPROLOL)	; Ongoing											
23. OTHER RELEVANT HIS	STORY. (e.g. diagnostics,	allergies, pregnancy with last mo	onth of period,										
Unknown to Ongoir	ng	Relevant Med His	story	Description Chronic	myeloid leuk	aemia (C	Chronic m	yeloid	leuka	emia)			
		IV. MANUF	ACTUR			ON							
24a. NAME AND ADDRESS Pfizer Inc Stella Pietrafesa	OF MANUFACTURER			26. REI	MARKS								
66 Hudson Boulevar New York, NY 10001													
Phone: 212 733 404													
	24b. MFR CC	NTROI NO		25b, NA	ME AND ADDRES	SS OF REPO	RTFR						
		0165375			E AND ADDR								
24c. DATE RECEIVED BY MANUFACTURER	24d. REPOR			NAM	AND ADDR	ESS WIT	HHELD.						
03-OCT-2023	Malana	LITERATURE OTHER:											
DATE OF THIS REPORT	PROFES 25a. REPOR	SSIONAL L		\dashv									
28-FEB-2024	⋈ INITIAL	FOLLOWUP:											

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 bosulinib. The reporter considered "skin lesions of the forehead and scalp" not

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.



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SUSPECT ADVERSE REACTION REPORT																					
			T		$\overline{}$	Γ	П	Т	\neg	\neg	Т	Т	Т	Г							
				И				\perp	$oldsymbol{\perp}$	\perp	\perp										
I. REACTION INFORMATION																					
PATIENT INITIALS (first, last)	(first, last)								ET Year												
PRIVACY PRIVACY Years Male 67.00 MAY 2021												1 ADVERSE REACTION									
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)								PATIENT DIED													
HYPOSIDEREMIA [Iron deficiency] decrease in breath sounds [Breath sounds abnormal]								INVOLVED OR PROLONGED INPATIENT													
Case Description: OBSERVATIONAL STUDY- EVALUATION OF EFFICACY AND SAFETY OF BOSULIF								HOSPITALISATION													
UNDER REAL-LIFE CONDITIONS OF USE							[_	OR S	OLVED I	ICAN	NT	ENT								
This is a non-interventional study report (Post Authorization Safety Study) received from a Physician and an								DISABILITY OR INCAPACITY													
Other HCP for protocol B1871047.																					
(Continued on Additional Information Page) L	LIFE THREATENING											
		II. SUSPEC	T DRUC	G(S) IN	FORMATIO	N															
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet						20. DID REACTION ABATE AFTER STOPPING DRUG?															
#1) Bosum (Bood Hivis) 1 impedated tablet						_ Drog!															
				i. ROUTE(S) 1) Unkno	YES NO NA																
17. INDICATION(S) FOR USE						21. DID REACTION															
#1) Unknown											AR AFT										
			. THERAPY DURATION 1) Unknown							YES NO NA											
#1) 06-NOV-2019 / Ongoing #1					,, ss																
		III. CONCOMIT	ANT DI	RUG(S) AND HIST	OR	Υ														
22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)																					
· · · · · · · · · · · · · · · · · · ·																					
23. OTHER RELEVANT HIS From/To Dates	STORY. (e.g. diagnostics,	allergies, pregnancy with last mor		etc.) Description																	
Unknown to Ongoin	ng	Relevant Med His			myelogenous l	euke	emia	(Chro	nic	mye	loid	l leu	ıkaen	nia)						
												—									
24a. NAME AND ADDRESS	S OF MANUFACTURED	IV. MANUF	ACTUR	ER INI		N_						—									
Pfizer Inc Stella Pietrafesa					IARRO																
66 Hudson Boulevard East New York, NY 10001 UNITED STATES																					
Phone: 212 733 404		7																			
	24b. MFR CO	NTROL NO.		25b. NA	ME AND ADDRESS	OF RE	PORTI	ER						_							
	PV202300165379 NAME AND ADDRESS V																				
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT	SOURCE		NAME AND ADDRESS WITHHELD.																	
06-DEC-2023	STUDY HEALTH PROFES																				
DATE OF THIS REPORT	25a. REPORT			\dashv																	
28-FEB-2024	⊠ INITIAL	FOLLOWUP:																			

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.

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SUSPE	CT ADVERSE F															٦					
				П	4	T	T	Τ		П	П		T		\exists						
							И						Ш					Ш			
1. PATIENT INITIALS	MATION 3a. WEIGHT	4-6 F	EACTI	ON OI	NSET	- 1	8-12	CF	HECK A	ALL.											
(first, last) PRIVACY	3. SEX 3a. WEIGHT 4-6 REACTION ONSET 8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION ADVERSE REACTION																				
7 + 13 DESCRIBE REAC Event Verbatim [PREFER hiatal hernia [Hia Evolutive esopha	PATIENT DIED INVOLVED OR PROLONGED INPATIENT HOSPITALISATION																				
Case Description UNDER REAL-LI	FICACY	FICACY AND SAFETY OF BOSULIF											VED PERSISTENT GNIFICANT								
This is a non-interventional study report (Post Authorization Safety Study) received from contactable reporter(s) (Physician and Other HCP) for protocol B1871047.									DISABILITY OR INCAPACITY												
				(Conti	nued on Addi	tional	nform	ation	n Pa	ge)] LIF	E IREATI	≣NIN	G						
		II. SUSPEC	T DRU	G(S) IN	FORMAT	ION															
14. SUSPECT DRUG(S) (include generic name) #1) Bosulif (BOSUTINIB) Film-coated tablet				(Conti		20. DID REACTION ABATE AFTER STOPPING DRUG?															
					ROUTE(S) OF ADMINISTRATION) Unknown								YES NO NA								
17. INDICATION(S) FOR USE #1) Unknown													21. DID REACTION REAPPEAR AFTER REINTRODUCTION?								
					THERAPY DURATION) 22 days								YES NO NA								
		III. CONCOMIT	TANT D	RUG(S) AND HIS	STO	۲Y														
		IINISTRATION (exclude those us HYDRATE) ; 18-JUL-2		-																	
23. OTHER RELEVANT	HISTORY. (e.g. diagnostics,	allergies, pregnancy with last mo	onth of period,	etc.)														\dashv			
From/To Dates Unknown to Ongo	oing	Type of History / Notes Relevant Med His		Description CML (Ch	ronic myelo	id leul	kaem	ia)													
		1) / MANUE	ACTUE	סרט ואונ		ON															
24a. NAME AND ADDRE	EER INFORMATION 26. REMARKS																				
Pfizer Inc Stella Pietrafesa 66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	3																			
	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDRE	SS OF F	REPOR	TER										\dashv			
	PV202300165408						NAME AND ADDRESS WITHHELD.														
24c. DATE RECEIVED BY MANUFACTURE	ER 24d. REPOR	SOURCE LITERATURE		NAME AND ADDRESS WITHHELD.																	
03-OCT-2023	HEALTH PROFES	HEALTH PROFESSIONAL OTHER:																			
DATE OF THIS REPORT 28-FEB-2024																					

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	Result not provided	
	tract		
14-19. SUSPECT DRUG(S) continue	d		
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-co	pated tablet; 100 mg, daily; Unknown	Unknown	20-JUN-2016 /
Regimen #2			26-JUN-2016;
			7 days

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SUSPE	CT ADVERSE F	REACTION REPO	RT																	
							П	T				Т	T	Τ		T	Τ			
							И	<u> </u>		Ш		Ц		丄						
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION 2a, AGE	INFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	ON ONS	EFT	T ₈₋₁	8-12 CHECK ALL									
(first, last) PRIVACY	(first, last) FRANCE Day Month Year 78 64.00 Day Month Year										APPROPRIATE TO									
	CTION(S) (including relevant RRED TERM] (Related symples Is [Erosive duodenit	tests/lab data) otoms if any separated by comma tis]	as)							ı		INVC	ENT DI	OR						
	: OBSERVATIONAL	L STUDY - EVALUATION	ON OF EF	FICACY	AND SAFE	TY OF	BOS	ULIF	:			PRO	LONGE	ED II SATI	ION					
This is a non-inte	, ,	port received from cont	actable re	eporters (Physician a	nd Oth	ner H0	CP) fo	or	[_	OR S	OLVED SIGNIFI ABILITY APACIT	ICAN 'OR	NT	ENT				
A 78-year-old ma	le patient received	bosutinib (BOSULIF), f	irst regim		nued on Addi	tional I	nforma	ation F	Page) 		LIFE THR		IING						
(Continued on Additional Information Page) UTHREATENING II. SUSPECT DRUG(S) INFORMATION																				
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name) JTINIB) Film-coated			, ,	nued on Addi		nform	ation F	Page			ATE A	CTION AFTER S		PPIN	3				
15. DAILY DOSE(S) #1) 200 mg, daily				6. ROUTE(S) 11) Unkno	OF ADMINISTRA	ATION						YES	i 🗆 N	10	⊠⊦	IA				
17. INDICATION(S) FOR #1) Chronic myelo		c myeloid leukaemia)								21.	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?									
18. THERAPY DATES(fro #1) 23-MAY-2016	•			9. THERAPY 1) 22 day								YES	: <u>П</u> и	10	⊠⊦	IA				
		III. CONCOMIT	TANT D	RUG(S) AND HIS	STOF	RY													
		MINISTRATION (exclude those us HYDRATE) ; 18-JUL-2																		
23. OTHER RELEVANT I	HISTORY, (e.g. diagnostics.	allergies, pregnancy with last mo	onth of period.	. etc.)																
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med His		Description	myeloid leuk	kemia	(Chro	nic m	nyelo	oid le	euka	aem	nia)							
														—						
IV. MANUFACTURER INFORMATION 24a. NAME AND ADDRESS OF MANUFACTURER 26. REMARKS												_								
Pfizer Inc Stella Pietrafesa 66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	S																		
	24b. MFR CC	NTROL NO.			ME AND ADDRE															
		00165540			AND ADDR															
24c. DATE RECEIVED BY MANUFACTURE	ER 24d. REPORT	T SOURCE LITERATURE		INAME	AND ADDR	.⊏35 V	vii Mf	iELD.												
03-OCT-2023	HEALTH PROFES			_																
25a. REPORT TYPE 28-FEB-2024 Initial Followup:																				

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. 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;	100 mg, daily; Unknown	Chronic myeloid leukemia	20-JUN-2016 / 26-JUN-2016:
Regimen #2		(Chronic myeloid leukaemia)	20-JUN-2010;
			7 days

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SUSPEC	T ADVERSE F	REACTION REPO	RT														
						Т		$\overline{}$	Π	П				Т	Т	T	Π
							14										
		I. REAC	CTION	INFOR	MATION												
PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 59	3. SEX	_	4-6 RI	Mont	_	ET Year	_	12	APP	CK ALL ROPRIA	ATE			
PRIVACY	TRANCE	PRIVACY	Years	Male	kg kg		FEE	3 2	02	0		ADV	ERSE F	REAG	STION	1	
· ·	RED TERM] (Related sym	otoms if any separated by commas	s)									PATI	ENT DII	ED			
Skin and hips crar eyelid edema [Eye		ns]										PRO	DLVED (D IN		ENT	
Case Description:	OBSERVATIONA	L STUDY - EVALUATIO	N OF FF	FICACY	AND SAFETY	′ OF	BOS	ULIF				HOS	PITALIS	SATI	ON		
UNDER REAL-LIF			NOI LI	TIOAGT	AND OAI ETT	01	ВОО	OLII				OR S	OLVED F	CAN	SISTE IT	NT	
		oort (Post Authorization		tudy) rec	eived from co	ntact	able						ABILITY				
reporter(s) (Physic	cian and Other HC	P) for protocol B187104	17.								_						
				(Conti	nued on Additio	nal Ir	nforma	tion F	age	e)	<u>Ц</u>	LIFE	EATENI	ING			
		II. SUSPEC	T DRU	G(S) IN	FORMATIC	N											
14. SUSPECT DRUG(S) (I #1) Bosulif (BOSU	-	tablet								20	AB		CTION FTER S	STO	PPINC	3	
#2) IMATINIB (IMA	,				nued on Additio	$\overline{}$	nforma	tion F	age)	DK	UG!					
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK			#	s. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRATION	ON						YES	i □ N	0	×	A	
17. INDICATION(S) FOR U #1) Unknown #2) chronic myeloid		: myeloid leukaemia)								21	21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(from #1) 15-JAN-2019 / #2) 14-JAN-2020 /	m/to) 18-FEB-2019		#	o. THERAPY 1) 1 mon 2) Unkno	th 4 days							YES	. . .	0	×Ν	Α	
		III. CONCOMIT	ANT DI	RUG(S) AND HIST	OR	Υ										
22. CONCOMITANT DRUG	G(S) AND DATES OF ADM	IINISTRATION (exclude those use			,												
23. OTHER RELEVANT H	ISTORY. (e.g. diagnostics,	allergies, pregnancy with last mor		etc.) Description													
Unknown to Ongo	ing	Relevant Med His			myeloid leukei	mia (Chro	nic m	iyel	oid l	euk	aem	nia)				
IV. MANUFACTURER INFORMATION 24a. NAME AND ADDRESS OF MANUFACTURER 26. REMARKS																	
Pfizer Inc Stella Pietrafesa	SS OF MANUFACTURER			26. REN	IARKS												
66 Hudson Bouleva New York, NY 1000		3															
Phone: 212 733 40		7															
	24b. MFR CC	NTROL NO.		25b. NA	ME AND ADDRESS	OF RI	EPORT	ER									
	The state of the s	0168896			AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR			NAME	AND ADDRES	SS W	/ITHH	ELD.									
10-OCT-2023	STUDY	LITERATURE OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR																

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet	; 300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet	; 200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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SUSPECT ADVERSE REACTION REPORT												_		_				
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							И						丄					
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION 2a. AGE	INFOR 3. SEX	MATION 3a. WEIGHT	400	EACTIC	N ONG	·	Taa	0 0		OK 411					
PRIVACY	FRANCE	Day Month Year PRIVACY	59 Years	Male	85.00	9ay 08	Mont API	h	Year 2020	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION								
DYSPNEA [Dyspi		t tests/lab data) ptoms if any separated by comma	as)							1	PATIENT DIED INVOLVED OR PROLONGED INPATIENT							
	: OBSERVATIONA FE CONDITIONS (L STUDY- EVALUATIO OF USE	N OF EF	FICACY	AND SAFETY	OF	BOSI	JLIF		<u>ן</u>	_ ⊒ ;;	NVO OR S	PITALIS DLVED I SIGNIFI	PER ICAN	SISTE	NT		
		port (Post Authorization P) for protocol B18710		tudy) rec	eived from co	ntac	table						BILITY PACIT					
				(Conti	nued on Additio	onal li	nforma	ation F	Page)	, [LIFE THRE	EATEN	IING				
		II. SUSPEC	T DRU	G(S) IN	FORMATIC	ON												
14. SUSPECT DRUG(S) #1) Bosulif (BOSU #2) IMATINIB (IMATINIB)	JTINIB) Film-coated	tablet		(Conti	nued on Additio	onal li	nforma	ation F	Page)			TE A	CTION FTER S		PPING	i		
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK			#	s. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRATI WN	ION						YES	□N	Ю	×Σ	A		
	id leukaemia (Chron	nic myeloid leukaemia) c myeloid leukaemia)								21.	REA	PPE	CTION AR AFT ODUCT	TER	?			
18. THERAPY DATES(fro #1) 15-JAN-2019 #2) 14-JAN-2020	/ 18-FEB-2019		#	o. THERAPY 1) 1 mon 2) Unkno	th 4 days							YES	Пν	Ю	×Σ	Ą		
		III. CONCOMIT	TANT D	RUG(S) AND HIS	TOF	RΥ											
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	action)														
OR OTHER RELEVANT	UIOTODY (E e											_		_				
From/To Dates Unknown to Ongo		, allergies, pregnancy with last mo Type of History / Notes Relevant Med His		Description	myeloid leuke	mia i	(Chro	nic m	velc	oid le	euka	em	ija)					
Children to Chig	Sirig	Notati ind Til	, , , , , , , , , , , , , , , , , , ,	Om om o	ny olola loako		(00		., 0.0	na ic	Junu	0111	iu,					
IV. MANUFACTURER INFORMATION																		
24a. NAME AND ADDRESS OF MANUFACTURER Pfizer Inc Stella Pietrafesa																		
66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	S																
	24b. MFR CC	ONTROL NO. 00168909			ME AND ADDRESS AND ADDRES													
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR			NAME	AND ADDRE	SS W	/ITHH	IELD.										
06-DEC-2023	STUDY HEALTH PROFES	LITERATURE SSIONAL OTHER:																
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																		

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	chronic myeloid leukaemia	19-FEB-2019 /
Regimen #2		(Chronic myeloid leukaemia)	13-SEP-2019;
		,	6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	chronic myeloid leukaemia	15-OCT-2019 /
Regimen #3		(Chronic myeloid leukaemia)	29-NOV-2019;
			1 month 15 days

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SUSPECT AI	OVERSE REACTION REPOR	RT														
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						И				$oldsymbol{\perp}$	$oldsymbol{\perp}$		\perp			
	I. REAC	CTION II	NFORM	MATION												
(first, last)	COUNTRY 2. DATE OF BIRTH Pay Month Year	2a. AGE 60	3. SEX	3a. WEIGHT Da		ACTIO	_	ET Year	8-1		APP	CK ALL	ATE T			
PRIVACY	PRIVACY	Years	Male		1	JAN	V 2	202	1		ADVI	ERSE F	REAC	HON		
	(including relevant tests/lab data) RM] (Related symptoms if any separated by commas	s)							1	J	PATI	ENT DII	ED			
worsening on coxarthro	sis [Osteoarthritis]								1	Δ	PRO	LVED (ED IN		NT	
Case Description: The in	nitial case was missing the following	ı minimum	criteria:	no event.							HOS	PITALIS	SATIC	JN		
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						>						PACIT				
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			(Contin	ued on Addition	nal Ir	forma	tion F	Page	*) -	<u> </u>	THRI	EATENI	NG			
A4 CHODEOT DDUG(O) (included	II. SUSPEC	T DRUG	(S) INF	ORMATIO	N				100	DID	DEA	CTION				
14. SUSPECT DRUG(S) (include (#1) Bosulif (BOSUTINIB)										ABA		FTER S		PPING	i	
15. DAILY DOSE(S)		16.		ued on Addition OF ADMINISTRATION	_	forma	tion F	Page	*)		_					
#1) 200 mg, daily) Unknow			•					YES	□N	0	×Ν	Ą	
17. INDICATION(S) FOR USE #1) Unknown			///						21.	REA	APPE.	CTION AR AFT				
,									4	REII	NTRO	ODUCT	ION?	•		
18. THERAPY DATES(from/to) #1) 15-JAN-2019 / 18-FE	:B-2019) 1 montl						YES NO NA							
										_	_		_			
22 CONCOMITANT DRUG(S) AN	III. CONCOMIT			AND HIST	OR	Y										
	B) ; 14-JAN-2020 / Ongoing	sa to treat reac	dony													
			7													
OS OTHER RELEVANT HISTORY	(e.g. diagnostics, allergies, pregnancy with last mor	-4b -6i1 -	4-1													
From/To Dates Unknown to Ongoing	Type of History / Notes Relevant Med His	D	escription	yeloid leukem	nia ()	,										
Criminal to Crigoring	Tolovalii Mod Tilo	.0.,		y olola loakon	a ()											
	IV. MANUF	ACTURE	ER INF	ORMATIOI	N											
24a. NAME AND ADDRESS OF M Pfizer Inc			26. REMA													
Stella Pietrafesa 66 Hudson Boulevard Ea																
New York, NY 10001 UN Phone: 212 733 4045	ITED STATES															
	24b. MFR CONTROL NO.		25h NAN	E AND ADDRESS	OE D'	ידמ סם:	ED.									
	24b. MFR CONTROL NO. PV202300168914			AND ADDRESS												
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE		NAME	AND ADDRES	S W	'ITHH	ELD.									
06-DEC-2023	STUDY LITERATURE HEALTH PROFESSIONAL OTHER:															
DATE OF THIS REPORT	25a. REPORT TYPE		-													
28-FEB-2024																

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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					MATION	4											
1. PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 59	3. SEX		ay	Mont	h	Year	8-1:	1	APPF	CK ALL ROPRIA ERSE F	ATE		ı	
PRIVACY	_	PRIVACY	Years	Male	kg 2	20	API	₹ 2	2020	4	,		INOLI	_/\	01101	•	
		t tests/lab data) ptoms if any separated by comma	ıs)							1	J '	PATI	ENT DI	ED			
COVID-19 infection		nctival haemorrhage]								C	_ ,	PRO	LONGE PITALIS	ED IN		ENT	
		L STUDY EVALUATION	N OF EFF	FICACY A	ND SAFETY	OF E	BOSL	LIF		_			7				
UNDER REAL-LI	FE CONDITIONS (OF USE								[OR S DISA	OLVED SIGNIFI ABILITY	ICAN 'OR	١T	NT	
		port (Post Authorization P) for protocol B18710		tudy) red	eived from co	ntac	table				ı	NCA	APACIT	Y			
		, ,		(Conti	nued on Additio	nal li	nforms	tion F	/ane	[LIFE	EATEN	IING			
		II CLICDEO	T DDL1/				11011116		age			TINI	EATEN	ING			
14. SUSPECT DRUG(S)	(include generic name)	II. SUSPEC	I DRU	NII (ح)د	FORMATIC	N				20.			CTION				
#1) Bosulif (BOSU #2) IMATINIB (IMATINIB)	JTINIB) Film-coated ATINIB)	tablet		(Conti	nued on Additio	nal li	nforma	ition F	Page)		DRU		FTER	510	PPING	j	
15. DAILY DOSE(S) #1) 200 mg, daily	,			5. ROUTE(S)	OF ADMINISTRATI	ION				1	П	YES	Пм	10	M	A	
#2) UNK				2) Oral	WII					ļ	_						
17. INDICATION(S) FOR #1) Unknown #2) Acute myeloid	use Heukemia (Acute my	yeloid leukaemia)								21. DID REACTION REAPPEAR AFTER REINTRODUCTION?							
18. THERAPY DATES(fro #1) 15-JAN-2019 #2) 14-JAN-2020	/ 18-FEB-2019		#	9. THERAPY 1) 1 mon 2) Unkno	th 4 days					YES NO NA							
		III. CONCOMIT	TANT D	RUG(S) AND HIS	TOF	RΥ										
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	action)													
From/To Dates		, allergies, pregnancy with last mo Type of History / Notes	•	Description		:-	(Ob ===			حالد:			.:_\				
Unknown to Ongo	oing	Relevant Med His	story	Chronic	myeloid leuke	mia	(Cnro	nic it	iyelo	іа іє	euka	em	la)				
IV. MANUFACTURER INFORMATION																	
24a. NAME AND ADDRE Pfizer Inc	SS OF MANUFACTURER			26. REN	IARKS												
Stella Pietrafesa 66 Hudson Boulev																	
New York, NY 100 Phone: 212 733 40	01 UNITED STATE: 045	S															
	24b. MFR CO	ONTROL NO.		25b. NA	ME AND ADDRESS	OF R	EPORT	ER				_		_			
		00169049			AND ADDRES												
24c. DATE RECEIVED BY MANUFACTURE	24d. REPOR	T SOURCE		NAME	AND ADDRE	SS W	/ITHH	ELD.									
10-OCT-2023	■ STODY ■ HEALTH PROFES	ш															
DATE OF THIS REPORT 25a. REPORT TYPE 28-FEB-2024 INITIAL FOLLOWUP:																	

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 leukaemia" (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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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SUSPECT ADV	/ERSE REACTION REPO	RT														
					T		$\overline{}$	Γ	П	\neg		$\overline{}$	Τ	Т	Ι	
						И				\Box						
	I. REA	CTION II	NFORI	MATION												
1. PATIENT INITIALS 1a. CC (first, last)	DUNTRY 2. DATE OF BIRTH Day Month Year	2a. AGE 58	3. SEX	3a. WEIGHT Da		ACTIO	N ONS	ET Year	8-		APP	CK ALL	ATE T			
PRIVACY	PRIVACY	Years	Male		5	MAI	₹ 2	01	9		ADV	ERSE F	REAC	HON		
-	(Related symptoms if any separated by comma	ıs)									PATI	ENT DII	ED			
Increase lipasemia [Lipase Thoracic pain [Chest pain]	-										PRO	LONGE	D IN		NT	
Case Description: OBSER	VATIONAL STUDY EVALUATION	N OF FFFI	CACY A	ND SAFETY (OF F	SOSU	l IF				HOS	PITALIS	SATIC	ON		
UNDER REAL-LIFE CONI		VOI LIII	OAOT A	IND OAI ETT	,	,000					OR S	OLVED F	CAN'	SISTE T	NT	
	This is a non-interventional study report (Post Authorization Safety Study) received from a Physician and an Other HCP for protocol B1871047.											ABILITY APACIT				
Other HCP for protocol B1871047.																
			(Conti	nued on Addition	nal In	forma	tion P	age	e)		LIFE	EATENI	ING			
	II. SUSPEC	T DRUG	S(S) IN	FORMATIO	N											
14. SUSPECT DRUG(S) (include gene #1) Bosulif (BOSUTINIB) Fi	•								20	ABA		CTION FTER S	STOP	PING	i	
#2) IMATINIB (IMATINIB)				nued on Addition	_	forma	tion P	age)	DIN	UG!					
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK		#1	ROUTE(S)) Unkno) Oral	OF ADMINISTRATIC WN	ON						YES	N	0	X N	Ą	
17. INDICATION(S) FOR USE #1) Unknown #2) Chronic myeloid leuken	nia (Chronic myeloid leukaemia)								21	RE/	APPE	CTION AR AFT ODUCT		,		
18. THERAPY DATES(from/to) #1) 15-JAN-2019 / 18-FEB- #2) 14-JAN-2020 / Ongoing	-2019	#1	THERAPY I) 1 mont) Unkno	h 4 days							YES	N	0	⊠ N	A	
	III. CONCOMIT	TANT DR	RUG(S)	AND HIST	OR	Υ										
22. CONCOMITANT DRUG(S) AND D	ATES OF ADMINISTRATION (exclude those us															
23. OTHER RELEVANT HISTORY. (e. From/To Dates	g. diagnostics, allergies, pregnancy with last mo		etc.) Description													
Unknown to Ongoing	Relevant Med His			nyeloid leuken	nia (Chro	nic m	yel	oid le	euk	aem	nia)				
24a. NAME AND ADDRESS OF MANI	IV. MANUF	ACTURI	ER INF		N_											
Pfizer Inc Stella Pietrafesa	UFACTURER		26. REM	ARKS												
66 Hudson Boulevard East New York, NY 10001 UNITE	ED STATES															
Phone: 212 733 4045	ED OWNED															
	24b. MFR CONTROL NO.		25b. NAI	ME AND ADDRESS (OF RE	PORTI	ER			—						
	PV202300169051			AND ADDRES												
24c. DATE RECEIVED 24d. REPORT SOURCE NAME AND ADDRESS WITHHEL																
06-DEC-2023	STUDY LITERATURE HEALTH PROFESSIONAL OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TYPE NINITIAL FOLLOWUP:															

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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SUSPE	CT ADVERSE I	REACTION REPO	RT														
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						_	И							丄			<u> </u>
1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION 2a. AGE	INFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONS	SET	8-1	2	CHE	CK ALI	_			
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	59 Years	Male	85.00	ay 8	Mont FEE	h	Year 2020	1		APP	ROPRI	IATE		N	
	creatinine [Blood o	t tests/lab data) ptoms if any separated by comma creatinine increased]	as)							1		INVO PRO	ENT D LVED LONG PITALI	OR ED I	NPAT	ENT	
UNDER REAL-LI	FE CONDITIONS							JLIF		INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY							
		port (Post Authorization P) for protocol B18710		tudy) rec	eived from co	ntac	able			 				Y			
	(Continued on Additional Information Page)											LIFE THR	EATEN	IING	6		
A SUSPECT PRUSON		II. SUSPEC	T DRU	G(S) IN	FORMATIC	<u>NC</u>				Las	DID	DEA	OTION	_			
#1) Bosulif (BOSU	II. SUSPECT DRUG(S) INFORMATION I. SUSPECT DRUG(S) (include generic name) 1) Bosulif (BOSUTINIB) Film-coated tablet 2) IMATINIB (IMATINIB) (Continued on Additional Information Page)												CTION FTER		PPIN	Э	
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK	2) IMATINIB (IMATINIB) (Continued on Additional Information Page) 5. DAILY DOSE(S) 1) 200 mg, daily (Continued on Additional Information Page) 16. ROUTE(S) OF ADMINISTRATION #1) Unknown											YES		10	×.	IA	
17. INDICATION(S) FOR #1) Unknown #2) Chronic myeld		Chronic myeloid leukaem	ia)							21.	REA	PPE	CTION AR AF ODUC	TER			
18. THERAPY DATES(fro #1) 15-JAN-2019 #2) 14-JAN-2020	/ 18-FEB-2019		#	9. THERAPY 1) 1 mon 2) Unkno	th 4 days							YES	- <u> </u>	۷O	×	IA	
		III. CONCOMIT	TANT D	RUG(S) AND HIST	ГОБ	Υ										
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	MINISTRATION (exclude those us	sed to treat rea	action)													
22 OTHER RELEVANT	HISTORY (a.g. diagnostics	, allergies, pregnancy with last mo	onth of poriod	oto)										_			
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med His		Description	myelogenous	leuk	emia	(Chro	onic	mye	eloid	l leu	ıkaeı	mia	a)		
		IV. MANUF	ACTUR	ER IN	ORMATIO	N											
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																	
24b, MFR CONTROL NO. 25b. NAME AND ADDRESS OF REPORTER NAME AND ADDRESS WITHHELD.																	
24c. DATE RECEIVED 24d. REPORT SOURCE NAME AND ADDRESS WITHHELD.																	
10-OCT-2023	STUDY MEALTH PROFE	LITERATURE OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR	T TYPE															

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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SUSPEC	T ADVERSE F	REACTION REPO	RT									_					
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							И					\perp					
					MATION												
1. PATIENT INITIALS (first, last)	1a. COUNTRY FRANCE	2. DATE OF BIRTH Day Month Year	2a. AGE 59	3. SEX	3a. WEIGHT 85.00	4-6 R Day	Mont	h	Year	8-1	Α	PPR	K ALL OPRIA RSE RI				
PRIVACY		PRIVACY	Years	Male	kg	A	JAN	1 2	2020	4	,,	J V L I	KOL IKI	L/101			
Event Verbatim [PREFER	TION(S) (including relevant RED TERM] (Related symp	t tests/lab data) ptoms if any separated by comma	ıs)							[J P	ATIE	NT DIE	D			
cough [Cough] MYALGIA [Myalgi	a]									C	_ P	ROL	VED O ONGEI) INPA		ΝT	
		L STUDY- EVALUATIO	N OF EFF	FICACY	AND SAFETY	OF	BOSI	JLIF									
UNDER REAL-LIF	FE CONDITIONS (OF USE								[- 0	R SIG	VED P GNIFIC BILITY (ANT OR	STEN	ΙT	
		port (Post Authorization P) for protocol B18710		tudy) red	eived from co	ontac	table				IN	ICAP	PACITY				
	(Continued on Additional Information Page)											IFE HRF	ATENIN	JG			
(Continued on Additional Information Page) II. SUSPECT DRUG(S) INFORMATION										<u> </u>	•						
14. SUSPECT DRUG(S) ((include generic name)	II. SUSPEC	IDRUC	5(S) IN	FORMATI	OIN				20.	DID R			TODD	1110		
#1) Bosulif (BOSU #2) IMATINIB (IMA	TINIB) Film-coated ATINIB)	tablet		(Conti	nued on Additi	onal l	nforma	ition F	Page)		DRUC		TER S	IOPP	ING		
15. DAILY DOSE(S) #1) 200 mg, daily	<u> </u>			. ROUTE(S)	OF ADMINISTRAT	TION				1	□Y	ES	NC	· E	NA		
#2) UNK 17. INDICATION(S) FOR	USE		#2	2) Oral						21.	DID R	EAC.	TION				\dashv
#1) Unknown		c myeloid leukaemia)									REAP	PEA	R AFTE				
18. THERAPY DATES(fro #1) 15-JAN-2019 / #2) 14-JAN-2020 /	18-FEB-2019		#-	. THERAPY 1) 1 mon 2) Unkno	th 4 days						ПΥ	ES	NC	>	NA		
		III. CONCOMIT	TANT DI	RUG(S) AND HIS	TOF	RΥ										
22. CONCOMITANT DRU	G(S) AND DATES OF ADM	MINISTRATION (exclude those us	ed to treat rea	ction)													
From/To Dates		allergies, pregnancy with last mo Type of History / Notes		Description			(0)						,				
Unknown to Ongo	oing	Relevant Med His	story	Chronic	myeloid leuke	emia	(Chro	nic m	iyelo	id le	ukae	mı	a)				
		IV. MANUF	ACTUR	ER INF	ORMATIC	DN.											
24a. NAME AND ADDRES	SS OF MANUFACTURER			26. REN													
Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard East																	
New York, NY 10001 UNITED STATES Phone: 212 733 4045																	
	24b. MFR CONTROL NO. 25b. NAME AND ADDRESS OF REPORTER																_
PV202300169614 PV202300169614 PV202300169614																	
24c. DATE RECEIVED 24d. REPORT SOURCE NAME AND ADDRESS WITHHELD.																	
10-OCT-2023	STUDY HEALTH PROFES	LITERATURE OTHER:															
DATE OF THIS REPORT 28-FEB-2024	25a. REPOR			1													

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. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Bosulif (BOSUTINIB) Film-coated tablet;	300 mg, daily; Unknown	Unknown	19-FEB-2019 /
Regimen #2			13-SEP-2019;
			6 months 26 days
#1) Bosulif (BOSUTINIB) Film-coated tablet;	200 mg, daily; Unknown	Unknown	15-OCT-2019 /
Regimen #3			29-NOV-2019;
			1 month 15 days

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SUSPE	CT ADVERSE F	REACTION REPO	RT											_				
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1. PATIENT INITIALS	1a. COUNTRY	I. REA	CTION I	3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONS	FT	8-1	12	CHE	CK ALL					
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	67	Female	98.00	Day 28	Mont MA	h	Year 2019	1		APPI	ROPRIA ERSE F	ATE		N		
Creatinine increa	CTION(S) (including relevant RRED TERM] (Related symp sed [Blood creatining Blood urea increase	•	s)							1		INVC PRO	DLVED (DLONGE	OR ED II		ENT		
	: OBSERVATIONA FE CONDITIONS (L STUDY - EVALUATIO DF USE	N OF EF	FICACY	AND SAFET	Y OF	BOS	ULIF		INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR								
	is is a non-interventional study report (Post Authorization Safety Study) received from contactable corter(s) (Physician and Other HCP) for protocol B1871047. (Continued on Additional Information Page)												APACIT'					
	(Continued on Additional Information Page)											LIFE	EATEN	ING	i			
		II. SUSPEC	T DRUC	G(S) IN	FORMATI	ON												
#1) Bosulif (BOSU #2) IMATINIB (IM.	JTINIB) Film-coated	tablet								20.		ATE A	CTION AFTER S		PPIN	3		
15. DAILY DOSE(S) #1) 200 mg, daily #2) UNK			#1	. ROUTE(S) 1) Unkno 2) Oral	OF ADMINISTRAT WN	TION						YES	S 🔲 N	Ю	×	IA		
	oid leukemia (Chronic	c myeloid leukaemia) c myeloid leukaemia)								21.	REA	APPE	CTION EAR AFT ODUCT	TER				
18. THERAPY DATES(fro #1) 29-APR-2019 #2) 02-FEB-2021	/ 16-SEP-2020		#1	. THERAPY 1) 1 year 2) Unkno	4 months 19	days						YES	S 🔲 N	Ю	⊠₁	IA		
		III. CONCOMIT	ANT DE	RUG(S	AND HIS	TOF	RΥ											
22. CONCOMITANT DRU	JG(S) AND DATES OF ADM	IINISTRATION (exclude those use	ed to treat rea	ction)														
22 OTHER RELEVANT	LIICTORY (a.g. diagnostics	allergies, pregnancy with last mo	nth of nariad	ata \														
From/To Dates Unknown to Ongo		Type of History / Notes Relevant Med His		Description	nyeloid leuke	emia ()											
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04 HULE HID ADDDS		IV. MANUF	ACTUR			NC												
Pfizer Inc Stella Pietrafesa 66 Hudson Boulev New York, NY 100																		
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24c. DATE RECEIVED BY MANUFACTURE	ER 24d. REPORT	SOURCE LITERATURE		INAME	AND ADDRE	.00 V	/II HH	CLV.										
13-OCT-2023	HEALTH PROFES																	
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:																

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.



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SUSPECT A	ADVERSE REAC	TION REPOR	Т																
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						Ц	4						\perp						
		I. REAC	TION II	NFOR	MATION														
(first, last)	RANCE Day	Month Year	67	3. SEX emale	98.00 Da 30	ıy	Month APF		Year		P	APPI	CK ALL ROPRIA ERSE F	ATE		1			
7 + 13 DESCRIBE REACTION(Event Verbatim [PREFERRED diarrheas [Diarrhoea] weight gain [Weight in	ERM] (Related symptoms if ar	data) ly separated by commas)	•			•				ı		NVC PRO	ENT DI	OR ED IN		≣NT			
Case Description: OB UNDER REAL-LIFE C	ONDITIONS OF USI							JLIF		INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY									
reporter(s) (Physician				udy) rece	eived iroin con	llact	able												
(Continued on Additional Information Page)												JIFE THRI	EATEN	ING					
		II. SUSPECT	DRUG	(S) IN	FORMATIO	N													
14. SUSPECT DRUG(S) (include #1) Bosulif (BOSUTINI										20.		TE A	CTION FTER S		PPING	€			
15. DAILY DOSE(S) #1) 200 mg, daily				ROUTE(S)) Unkno	OF ADMINISTRATIC WN	ON						YES	N	10	×Μ	A			
17. INDICATION(S) FOR USE #1) Chronic myelogene	ous leukemia (Chronic	myeloid leukaemia))							21.	REA	PPE	CTION AR AF1 ODUCT	TER	?				
18. THERAPY DATES(from/to) #1) 29-APR-2019 / On	going			THERAPY I								YES	Пи	Ю	×Μ	Α			
	III	. CONCOMITA	NT DR	RUG(S)	AND HIST	OR	Υ										,		
22. CONCOMITANT DRUG(S)	AND DATES OF ADMINISTRA	FION (exclude those used	to treat react	tion)															
23. OTHER RELEVANT HISTO From/To Dates	Ty	pe of History / Notes	D	escription															
Unknown to Ongoing	R	elevant Med Histo	ory C	Chronic r	nyelogenous le	euke	emia	(Chro	nic	mye	eloid	leι	ıkaen	nia))				
		IV. MANUFA	CTLIDE	ED INIE		NI.													
	MANUFACTURER	IV. WANUFA	CIUKE			N_													
24a. NAME AND ADDRESS OF MANUFACTURER Pfizer Inc Stella Pietrafesa 66 Hudson Boulevard East New York, NY 10001 UNITED STATES Phone: 212 733 4045																			
	24b. MFR CONTROL N	O.			ME AND ADDRESS (_					
PV202300170986 NAME AND ADDRESS WITHHELD. NAME AND ADDRESS WITHHELD.																			
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURC	LITERATURE		. 47 (171)		V V													
13-OCT-2023	HEALTH PROFESSIONAL	OTHER:																	
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT TYPE INITIAL	FOLLOWUP:																	

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.

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SUSPECT	· ADVERSE F	REACTION REPO	RT										
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		I RΕΔ(CTION	INIEOR	MATION								
1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX		6 REACTION ONSET	8-12 CHECK ALL						
PRIVACY	FRANCE	Day Month Year PRIVACY	67 Years	Female	98.00 Day 07		APPROPRIATE TO ADVERSE REACTION						
7 + 13 DESCRIBE REACTIO Event Verbatim [PREFERREI	N(S) (including relevant D TERM] (Related symp	tests/lab data) toms if any separated by comma	s)				PATIENT DIED						
Anemia [Anaemia] Cramps [Muscle spa	asms]						INVOLVED OR PROLONGED INPATIENT HOSPITALISATION						
		STUDY - EVALUATIO	N OF EF	FICACY	AND SAFETY	OF BOSULIF	WAY ONLY ED DEDOUGTENT						
UNDER REAL-LIFE	CONDITIONS)F USE					INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR						
This is a non-interve reporter(s) (Physicia		oort (Post Authorization	Safety S	tudy) rec	eived from cont	actable	INCAPACITY						
Teporter(s) (i riyaida	III) IUI PIUIUGUI D	107 1047.	4				LIFE						
	(Continued on Additional Information Page II. SUSPECT DRUG(S) INFORMATION												
•		II. SUSPEC	T DRUC	G(S) IN	FORMATION	N	T						
14. SUSPECT DRUG(S) (incl #1) Bosulif (BOSUTII	-		20. DID REACTION ABATE AFTER STOPPING DRUG?										
15. DAILY DOSE(S) #1) 200 mg, 1x/day		N .	YES NO NA										
17. INDICATION(S) FOR USE #1) Unknown	E						21. DID REACTION REAPPEAR AFTER REINTRODUCTION?						
18. THERAPY DATES(from/to #1) 29-APR-2019 / U	•			o. THERAPY 1) Unkno			YES NO NA						
		III. CONCOMIT	ANT DI	RUG(S) AND HISTO	DRY	1						
22. CONCOMITANT DRUG(S	S) AND DATES OF ADM	INISTRATION (exclude those use	ed to treat rea	action)									
	TORY. (e.g. diagnostics,	allergies, pregnancy with last mor											
From/To Dates Unknown to Ongoing	g	Type of History / Notes Relevant Med His		Description Chronic I	nyeloid leukem	ia (Chronic myelo	oid leukaemia)						
		IV. MANUE	ACTUR	FR INF	ORMATION								
24a. NAME AND ADDRESS (OF MANUFACTURER	171171111111111111111111111111111111111	7.010	26. REN		ı							
Stella Pietrafesa 66 Hudson Boulevard New York, NY 10001 Phone: 212 733 4045	UNITED STATES												
	24b. MFR COI				ME AND ADDRESS O								
24c DATE RECEIVED	24d. REPORT			NAME	AND ADDRESS	S WITHHELD.							
24c. DATE RECEIVED BY MANUFACTURER	⊠ STUDY	LITERATURE											
13-OCT-2023	HEALTH			_									
28-FEB-2024	25a. REPORT	TYPE FOLLOWUP:											

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.

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SUSPE	CT ADVERSE F	REACTION REPO	RT																		
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							И							上	<u> </u>		<u> </u>				
1. PATIENT INITIALS	1a. COUNTRY	I. REAC	CTION 2a. AGE	INFOR 3. SEX	MATION 3a. WEIGHT	4-6 R	EACTIO	N ONSI	FT	8-1:	2 C	HEC	CK ALL								
(first, last) PRIVACY	FRANCE	Day Month Year PRIVACY	69	Female	98.00	Day 04	Month MA	1	Year 021	1	Α	PPR	ROPRIA ERSE R								
Muscular cramps	CTION(S) (including relevant RRED TERM] (Related symp [Muscle spasms] sion flare-up [Hyper	tests/lab data) stoms if any separated by commastension]	s)							1		NVOI PROL	LVED C LONGE PITALIS	OR D INF		NT					
	: OBSERVATIONAL FE CONDITIONS (L STUDY - EVALUATIO OF USE	N OF EF	FICACY	AND SAFET	Y OF	BOS	ULIF		INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR											
	nis is a non-interventional study report (Post Authorization Safety Study) received from contactable porter(s) (Physician and Other HCP) for protocol B1871047. (Continued on Additional Information Page)										DISABILITY OR INCAPACITY										
												IFE HRE	ATENI	NG							
		II. SUSPEC	T DRU	G(S) IN	FORMATI	ON															
14. SUSPECT DRUG(S) #1) Bosulif (BOSU	(include generic name) JTINIB) Film-coated	tablet								20.	DID R ABAT DRUC	EAF	CTION FTER S	TOPE	PING						
15. DAILY DOSE(S) #1) 200 mg, daily				s. route(s) 1) Unkno	OF ADMINISTRAT	TION					ПΥ	ÆS.	□ N	> [2	3 N≠	١					
17. INDICATION(S) FOR #1) Chronic myelo		c myeloid leukaemia)								21.		PPEA	CTION AR AFT DUCTI								
18. THERAPY DATES(fro #1) 29-APR-2019	•			o. THERAPY 1)1 year	DURATION 4 months 19	days					ПΥ	/ES	NO	> [3 N≠						
		III. CONCOMIT	ANT D	RUG(S) AND HIS	TOF	RY														
	JG(S) AND DATES OF ADM	IINISTRATION (exclude those use 3-2021 / Unknown	ed to treat rea	action)																	
, ,																					
23. OTHER RELEVANT From/To Dates Unknown to Ongo		allergies, pregnancy with last mor Type of History / Notes Relevant Med His		Description	nyeloid leuke	emia i	(Chro	nic m	velo	id le	uka	emi	ia)								
Officiowit to Offigi	oing	Acievant wed ins	itory	Onionion	nyciola leak	ciiia	(01110)	1110 111	ycio	iu ic	unac	J1111	a)								
		IV. MANUF	ACTUR	ER INF	ORMATIC	NC															
Pfizer Inc	SS OF MANUFACTURER			26. REM	ARKS																
Stella Pietrafesa 66 Hudson Boulev New York, NY 100 Phone: 212 733 40	01 UNITED STATES	3																			
	24h MER CO	NTROL NO.		25b NA	ME AND ADDRES	S OF P	EPORT	ER													
	24b, MFR CONTROL NO. 25b. NAME AND ADDRESS OF REPORTER NAME AND ADDRESS WITHHELD.											D.									
24c. DATE RECEIVED BY MANUFACTURE	24d. REPORT	SOURCE LITERATURE		NAME	AND ADDRE	ESS W	/ITHH	ELD.													
13-OCT-2023	HEALTH PROFES																				
DATE OF THIS REPORT 28-FEB-2024	25a. REPORT	TTYPE FOLLOWUP:																			

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 leukaemia" (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.