Braftovi

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
PSUSA/10719 /202306	Periodic Safety Update EU Single assessment - encorafenib	25/01/2024	19/03/2024		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10719/202306.
IAIN/0038/G	This was an application for a group of variations.	05/03/2024	n/a		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer				
IB/0037	B.II.e.2.d - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition or replacement of a specification parameter as a result of a safety or quality issue	29/02/2024	n/a		
IB/0036	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	22/12/2023	n/a		
II/0031	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/12/2023	19/03/2024	SmPC	
IA/0033	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	26/09/2023	n/a		

R/0029	Renewal of the marketing authorisation.	26/04/2023	23/06/2023	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Braftovi in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0030/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	07/03/2023	n/a		
PSUSA/10719 /202206	Periodic Safety Update EU Single assessment - encorafenib	12/01/2023	n/a		PRAC Recommendation - maintenance
II/0026	Update of section 4.2 of the SmPC in order to introduce a new scheme of encorafenib dose reduction recommendations for the treatment of adult patients with unresectable or metastatic	23/06/2022	25/07/2022	SmPC and PL	

	melanoma with a BRAF V600 mutation, by replacing the second dose reduction level of 200 mg once daily by 225 mg once daily; based on results from simulation report (ARRA-CSC-104). In addition, the MAH took the opportunity to introduce an update of the user instructions in the Package Leaflet for increased clarity. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	23/03/2022	n/a		
IAIN/0025	A.1 - Administrative change - Change in the name and/or address of the MAH	24/01/2022	25/07/2022	SmPC, Labelling and PL	
PSUSA/10719 /202106	Periodic Safety Update EU Single assessment - encorafenib	13/01/2022	n/a		PRAC Recommendation - maintenance
IB/0024/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved	22/12/2021	n/a		

	manufacturer				
II/0020	Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with rosuvastatin and bupropion based on final results from Arm 2 of study ARRAY-818-103. This is a Phase 1, three-arm, open-label drug-drug interaction study in patients with BRAF V600-mutant unresectable or metastatic melanoma or other BRAF V600-E and/or K-mutant advanced solid tumours. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/10/2021	06/01/2022	SmPC	SmPC new text In vivo, encorafenib is an inhibitor of OATP1B1, OATP1B3 and/or BCRP. Coadministration of encorafenib with OATP1B1, OATP1B3 or BCRP substrates (such as rosuvastatin, atorvastatin, methotrexate) can result in increased concentrations. Repeated administration of encorafenib 450 mg once daily and binimetinib 45 mg twice daily with a single dose of rosuvastatin (a OATP1B1, OATP1B3 and BCRP substrate) increased rosuvastatin Cmax by 2.7-fold and AUC by 1.6-fold indicating a mild inhibition of OATP1B1, OATP1B3 and/or BCRP transporters.
IA/0022	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	25/08/2021	n/a		
IA/0021	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	09/08/2021	06/01/2022	SmPC	
PSUSA/10719 /202012	Periodic Safety Update EU Single assessment - encorafenib	08/07/2021	n/a		PRAC Recommendation - maintenance
IA/0019/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	31/03/2021	06/01/2022	Annex II and PL	

	Replacement/addition of a site where batch control/testing takes place				
PSUSA/10719 /202006	Periodic Safety Update EU Single assessment - encorafenib	14/01/2021	n/a		PRAC Recommendation - maintenance
IB/0015/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	13/01/2021	n/a		
IB/0017	B.II.e.1.a.1 - Change in immediate packaging of the	11/01/2021	06/01/2022	SmPC,	

	finished product - Qualitative and quantitative composition - Solid pharmaceutical forms			Labelling and PL	
IB/0014	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	14/12/2020	n/a		
IB/0016/G	This was an application for a group of variations. B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	09/12/2020	n/a		
IB/0011/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	04/09/2020	n/a		

IA/0012/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size	26/08/2020	n/a		
PSUSA/10719 /201912	Periodic Safety Update EU Single assessment - encorafenib	09/07/2020	n/a		PRAC Recommendation - maintenance
WS/1695	This was an application for a variation following a	30/04/2020	02/06/2020	SmPC, Annex	Please refer to Scientific Discussion Braftovi-H-C-4580-WS-

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Note: The MAH in the course of the assessment withdrew Mektovi (binimetinib) from the applied indication. Therefore, the extension of indication only concerns the product Braftovi (encorafenib). Extension of indication to include encorafenib in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy, as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 2.0 is acceptable. Furthermore, the PI is brought in line with the latest QRD template version 10.1. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one			II and PL	1695.
IA/0010/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or	11/05/2020	n/a		

	deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				

PSUSA/10719 /201906	Periodic Safety Update EU Single assessment - encorafenib	16/01/2020	n/a		PRAC Recommendation - maintenance
IAIN/0007/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	14/10/2019	02/06/2020	Annex II and PL	
PSUSA/10719 /201812	Periodic Safety Update EU Single assessment - encorafenib	11/07/2019	n/a		PRAC Recommendation - maintenance
IB/0004/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	23/04/2019	29/10/2019	SmPC and PL	
IAIN/0005	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer	11/04/2019	n/a		

	responsible for importation and/or batch release - Not including batch control/testing				
II/0002/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	31/01/2019	n/a		
IB/0001/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside	07/11/2018	29/10/2019	SmPC, Labelling and PL	

	the range of the currently approved pack sizes				