Lonsurf

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
IB/0029	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/04/2024	n/a		
PSUSA/10517 /202303	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	26/10/2023	n/a		PRAC Recommendation - maintenance

[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).

II/0026	Extension of indication to include treatment of patients with refractory metastatic colorectal cancer for LONSURF in combination with bevacizumab based on results from study SUNLIGHT (CL3-95005-007); This is an open-label, randomised, phase III study comparing trifluridine/tipiracil in combination with bevacizumab to trifluridine/tipiracil monotherapy in patients with refractory metastatic colorectal cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC. The package leaflet is updated in accordance. The updated RMP version 10 has also been submitted. In addition, the MAH took the opportunity to update section 4.6 of the SmPC and the Package leaflet accordingly. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/06/2023	26/07/2023	SmPC and PL	Please refer to Scientific Discussion 'Product Name-H-C-003897-II-0026
II/0025	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	15/06/2023	n/a		
IAIN/0027/G	This was an application for a group of variations. B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.1.b - Replacement or addition of a	24/05/2023	26/07/2023	Annex II and PL	

	manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IB/0024/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) A.7 - Administrative change - Deletion of manufacturing sites B.I.d.1.a.4 - Stability of AS - Change in the re-test	27/01/2022	n/a		

	period/storage period - Extension or introduction of a re-test period/storage period supported by real time data 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.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/09/2021	26/07/2023	PL	
IB/0022	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	09/04/2021	n/a		
IAIN/0021	B.III.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	08/02/2021	n/a		

R/0020	Renewal of the marketing authorisation.	15/10/2020	14/12/2020	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Lonsurf in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10517 /202003	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0016	Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with severe renal impairment based on final results from study TO-TAS-102-107 (A Phase 1, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAS-102 in Patients With Advanced Solid Tumors and Varying Degrees of Renal Impairment). The Package Leaflet is updated accordingly. The updated RMP version 8.0 has also been agreed. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template revision 2 of the good Pharmacovigilance practice module V guideline and to align the PI to the QRD template version 10.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/02/2020	01/04/2020	SmPC and PL	For patients with severe renal impairment a starting dose of 20 mg/m2 twice daily is recommended. One dose reduction to a minimum dose of 15 mg/m2 twice daily is permitted based on individual safety and tolerability. Dose escalation is not permitted after it has been reduced. Administration is not recommended in patients with end stage renal disease as there are no data available for these patients. For more information please refer to the Summary of Product Characteristics.
IA/0018/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting	17/01/2020	n/a		

	material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
IA/0017/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method	31/10/2019	n/a		

	B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
PSUSA/10517 /201903	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	03/10/2019	n/a		PRAC Recommendation - maintenance
II/0012	Extension of Indication to include the treatment, as monotherapy, of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two systemic treatment regimens for advanced disease for Lonsurf; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 7.0 has also been submitted and updated in accordance with Template Rev 2. For clarification, the term monotherapy has also been added to the existing indication in metastatic colorectal cancer. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	25/07/2019	03/09/2019	SmPC and PL	Please refer to the published Assessment Report Lonsurf H-3897-II-0012.
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/07/2019	03/09/2019	PL	
IA/0013/G	This was an application for a group of variations.	03/04/2019	03/09/2019	Annex II and	

	A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter			PL	
PSUSA/10517 /201803	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	04/10/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10517 /201709	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	12/04/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10517 /201704	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	30/11/2017	n/a		PRAC Recommendation - maintenance
IB/0009	C.I.11.z - Introduction of, or change(s) to, the	17/11/2017	n/a		

	obligations and conditions of a marketing authorisation, including the RMP - Other variation				
IB/0008	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)	14/08/2017	07/03/2018	SmPC	
PSUSA/10517 /201610	Periodic Safety Update EU Single assessment - trifluridine / tipiracil	05/05/2017	n/a		PRAC Recommendation - maintenance
IA/0006	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	24/04/2017	n/a		
IAIN/0005/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.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	24/04/2017	07/03/2018	Annex II and PL	
II/0002/G	This was an application for a group of variations.	23/03/2017	07/03/2018	SmPC, Labelling and	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data			PL	
II/0003	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	16/03/2017	n/a		
IAIN/0001	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	27/07/2016	n/a		