Alofisel

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
R/0036	Renewal of the marketing authorisation.	10/11/2022	10/01/2023	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CAT and CHMP considered that the benefit-risk balance of Alofisel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. The MAH updated the RMP with the status of the ongoing Cx601 0303 study.

[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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					Annex A of Alofisel was updated in order to reflect correct QRD terminology. The product information was updated in accordance with the latest QRD template and minor wording clarifications have also been included. Further, the MAH will update section 4.8 of the SmPC in a separate procedure.
IB/0042/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.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	16/12/2022	n/a		
IB/0039/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	07/11/2022	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.z - Quality change - Active substance - Other variation				
IB/0041/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.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	03/10/2022	n/a		
IB/0040/G	This was an application for a group of variations. B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.z - Quality change - Finished product - Other variation	15/09/2022	n/a		
IB/0038	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	14/07/2022	n/a		

IB/0037	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	27/06/2022	n/a		
IB/0033	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	19/04/2022	n/a		
PSUSA/10676 /202109	Periodic Safety Update EU Single assessment - darvadstrocel	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0034/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	31/03/2022	n/a		
IA/0035/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	04/03/2022	n/a		

	changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0032	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/03/2022	10/01/2023	Annex II	To extend the due date for the Long Term Extension Study Cx601-0303 (ADMIRE-CD II Study) from 2Q/3Q 2022 to Q1/Q2 2024 in both the RMP and in the product information Annex II, as the enrolment has been significantly affected due to the COVID-19 pandemic. In addition the MAH has taken the opportunity to bring the annexes in line with QRD template (vers.10.2).
IB/0028/G	This was an application for a group of variations. 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	23/02/2022	n/a		
IB/0031	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	02/02/2022	n/a		
PSUSA/10676 /202103	Periodic Safety Update EU Single assessment - darvadstrocel	28/10/2021	n/a		PRAC Recommendation - maintenance

II/0027	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	16/09/2021	n/a		
IB/0025	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	21/06/2021	22/10/2021	Annex II and PL	
PSUSA/10676 /202009	Periodic Safety Update EU Single assessment - darvadstrocel	09/04/2021	n/a		PRAC Recommendation - maintenance
IA/0024	A.7 - Administrative change - Deletion of manufacturing sites	03/03/2021	n/a		
II/0021	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	28/01/2021	n/a		
IB/0023/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/01/2021	n/a		
IAIN/0020/G	This was an application for a group of variations.	30/11/2020	22/10/2021	SmPC,	

	A.6 - Administrative change - Change in ATC Code/ATC Vet Code A.1 - Administrative change - Change in the name and/or address of the MAH			Labelling and PL	
PSUSA/10676 /202003	Periodic Safety Update EU Single assessment - darvadstrocel	29/10/2020	n/a		PRAC Recommendation - maintenance
IB/0019	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	19/10/2020	22/10/2021	SmPC and PL	
IB/0018	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	28/07/2020	n/a		
II/0016/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.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	28/05/2020	n/a		

PSUSA/10676 /201909	Periodic Safety Update EU Single assessment - darvadstrocel	17/04/2020	n/a		PRAC Recommendation - maintenance
IB/0015	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	19/03/2020	n/a		
II/0010/G	This was an application for a group of variations. B.I.e.2 - Introduction of a post approval change management protocol related to the AS B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	27/02/2020	n/a		
II/0009	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	27/02/2020	n/a		
IA/0014	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/01/2020	27/03/2020	SmPC, Annex II, Labelling and PL	
IB/0012/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of	19/12/2019	n/a		

	specification limits 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				
IB/0008/G	This was an application for a group of variations. 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 B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	07/10/2019	27/03/2020	SmPC	
PSUSA/10676 /201903	Periodic Safety Update EU Single assessment - darvadstrocel	03/10/2019	n/a		PRAC Recommendation - maintenance
II/0006	Submission of an updated RMP version 7 in order to propose replacement of the observational PASS study (Category 3) with two separate studies: a long-term safety extension of the ADMIRE-CD II study and a retreatment PASS. The European multi-database linkage study is added for the assessment of the potential risk of tumorgenicity.	29/05/2019	n/a		Following EMA scientific advice this variation was to update the post authorisation follow up on effectiveness and safety as outlined in the RMP in order to more effectively assess long-term effectiveness and safety of darvastocel including repeat administration. The Pharmacovigilance plan was updated and Protocol synopses and on a 4 year extension of the ADMIRE II study, a dedicated re-treatment PASS and a European multi-database linkage study were agreed to

	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				replace the previously agreed re-treatment PASS.
PSUSA/10676 /201809	Periodic Safety Update EU Single assessment - darvadstrocel	11/04/2019	n/a		PRAC Recommendation - maintenance
IB/0005	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	05/04/2019	27/03/2020	SmPC, Labelling and PL	
IB/0002	B.II.e.z - Change in container closure system of the Finished Product - Other variation	16/08/2018	n/a		
IAIN/0003/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	12/07/2018	n/a		
T/0001	Transfer of Marketing Authorisation	18/04/2018	08/05/2018	SmPC,	

				Labelling and PL	