Trecondi

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/10777 /202306	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	11/01/2024	n/a		PRAC Recommendation - maintenance
R/0019	Renewal of the marketing authorisation.	09/11/2023	05/01/2024	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Trecondi in the approved indication remains favourable and

[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).

					therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0014	Extension of indication to include additional non-malignant transplant indications (non-malignant diseases in the paediatric population) for Trecondi 1 g/5 g powder for solution for infusion based on final 12-months follow-up results of study MC-FludT.16/NM; a randomised phase II interventional study aimed to compare Treosulfan-based conditioning therapy with Busulfan-based conditioning prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with non-malignant diseases. Further, the MAH proposes to amend an existing warning on skin toxicity based on new literature data. Moreover, the MAH proposes to introduce a slightly modified dosing regimen according to the patient's body surface based on long-term follow-up data of paediatric study MC-FludT.17/M, a Phase II trial to describe the safety and efficacy of Treosulfan based conditioning therapy prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with haematological malignancies, as well as a final analysis of the population pharmacokinetics of treosulfan in paediatric patients. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) -	26/01/2023	06/03/2023	SmPC and PL	Please refer to Scientific Discussion Trecondi-H-C-004751/II/0014

	Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10777 /202206	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	12/01/2023	n/a		PRAC Recommendation - maintenance
II/0016	Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study MC-FludT.14/L Trial II; a phase III trial to compare Treosulfan-based conditioning therapy with Busulfan-based reduced-intensity conditioning (RIC) prior to allogeneic haematopoietic stem cell transplantation in patients with AML or MDS considered ineligible to standard conditioning regimens. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	10/11/2022	06/03/2023	SmPC and PL	Please refer to Scientific Discussion 'Trecondi-H-C-004751-II-0016' For more information, please refer to the Summary of Product Characteristics.
II/0012	Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with regards to CYP3A4, CYP2C19 and P-gp including physiologically based pharmacokinetic (PBPK) modelling. Version 1.1 of the RMP has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/10/2022	06/03/2023	SmPC	Not applicable Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-Var.No' SmPC new text For more information, please refer to the Summary of Product Characteristics.

II/0013	Update of section 5.3 of the SmPC in order to update the description of non-clinical information regarding musculoskeletal and connective tissue disorders in form of lympho-histiocytic infiltration in the skeletal muscles and renal and urinary disorders which show up as haematuria. These new determinations are based on results from study LPT 37259. A revised RMP version 1.2 was submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/09/2022	06/03/2023	SmPC	
IB/0017/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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	10/06/2022	n/a		
IA/0015	A.7 - Administrative change - Deletion of manufacturing sites	05/04/2022	n/a		
IA/0011/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	08/02/2022	n/a		

	changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
PSUSA/10777 /202106	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	13/01/2022	n/a		PRAC Recommendation - maintenance
IB/0010	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	03/12/2021	n/a		
PSUSA/10777 /202012	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	08/07/2021	n/a		PRAC Recommendation - maintenance
PSUSA/10777 /202006	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	14/01/2021	n/a		PRAC Recommendation - maintenance
IB/0006	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	21/12/2020	n/a		
II/0004/G	This was an application for a group of variations. 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 B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting	24/09/2020	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 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.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) B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS 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.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				
II/0003/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation 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 B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a	23/07/2020	10/11/2020	SmPC, Annex II and PL	

	new specification parameter to the specification with its corresponding test method B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification 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 B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test				

	procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.f.1.b.3 - Stability of FP - Extension of the shelf life of the finished product - After dilution or reconstitution (supported by real time data)				
PSUSA/10777 /201912	Periodic Safety Update EU Single assessment - treosulfan (for centrally authorised product)	09/07/2020	n/a		PRAC Recommendation - maintenance
IB/0001	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	10/03/2020	01/04/2020	SmPC, Annex II and PL	