Reblozyl

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/0031	Renewal of the marketing authorisation.	12/12/2024	14/02/2025	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Reblozyl in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.

[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).

PSUSA/10860 /202406	Periodic Safety Update EU Single assessment - luspatercept	16/01/2025	n/a		PRAC Recommendation - maintenance
II/0028	Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on results from Study ACE-536-MDS-002 following procedure EMEA/H/C/004444/II/0021. This is a phase 3, open-label, randomized study to compare the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R very low, low, or intermediate risk myelodysplastic syndromes (MDS) in ESA naive subjects who require red blood cell transfusions. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/09/2024	14/02/2025	SmPC	Update of section 5.2 of the SmPC to update pharmacokinetic information based on results from study ACE-536-MDS-002, a phase 3, open-label, randomized study to compare the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R very low, low, or intermediate risk myelodysplastic syndromes (MDS) in ESA naive subjects who require red blood cell transfusions. a serious breach of the study protocol was identified for study ACE-536-MDS-002 (COMMANDS). This follows the evaluation of procedure EMEA/H/C/004444/II/0021 where a serious breach was related to the collection, in error, of more than 3000 biological samples (including blood and urine), in excess of what was specified in the protocol and the informed consent form. Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-Var.No' For more information, please refer to the Summary of Product Characteristics.
IB/0030	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	22/08/2024	n/a		
IA/0029	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	23/07/2024	n/a		
II/0027	B.I.b.2.d - Change in test procedure for AS or	11/04/2024	n/a		

	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				
II/0021	Extension of indication to include treatment of adult patients with transfusion-dependent anaemia due to very low, low and intermediate-risk myelodysplastic syndromes (MDS), based on results from study ACE-536-MDS-002 (COMMANDS), an active-controlled, open-label, randomized Phase 3 study comparing the efficacy and safety of luspatercept vs epoetin alfa in adult subjects with anemia due to IPSS-R very low, low or intermediate risk MDS, who are ESA naïve and require RBC transfusions, and studies ACE-536-MDS-001(MEDALIST), ACE-536-MDS-004 , A536-03, A536-05 and ACE-536-LTFU-001; 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. Version 2.1 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/02/2024	27/03/2024	SmPC and PL	Extension of indication to include treatment of adult patients with transfusion-dependent anaemia due to very low, low and intermediate-risk myelodysplastic syndromes (MDS), based on results from study ACE-536-MDS-002 (COMMANDS). Please refer to Scientific Discussion 'Product Name-H-C-4444-II-21'.
PSUSA/10860 /202306	Periodic Safety Update EU Single assessment - luspatercept	11/01/2024	n/a		PRAC Recommendation - maintenance
II/0023	Submission of the final report from study ACE-536-MDS-005 listed as a category 3 study in the RMP.	11/01/2024	27/03/2024	SmPC, Annex	Update of the Product Information and Risk Management Plan to refer to the patient card for women for childbearing

	This is a non-interventional post-authorisation safety study (PASS) to evaluate the effectiveness of the additional risk minimisation measure (aRMM) for Reblozyl among Healthcare Providers (HCPs) in the EU/EEA. Update of section 4.6 of the PI and Annex II.D. The Package Leaflet has been updated accordingly. The RMP version 3.2 has been submitted accordingly. 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			II and PL	potential. In addition, the HCPs checklist has been kept and should be made available in the concerned Member States. For more information please refer to the Summary of Product Characteristics.
IB/0026/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 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	04/12/2023	n/a		
IA/0025/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 changes to an approved test procedure A.7 - Administrative change - Deletion of manufacturing sites	25/09/2023	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier				
IB/0022	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	24/08/2023	27/03/2024	SmPC	
PSUSA/10860 /202212	Periodic Safety Update EU Single assessment - luspatercept	06/07/2023	n/a		PRAC Recommendation - maintenance
II/0016	Please refer to the Recommendations section above. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/06/2023	27/03/2024	SmPC	
IB/0018/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	02/05/2023	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IB/0020/G	This was an application for a group of variations. B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	30/03/2023	n/a		
IB/0017/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	03/03/2023	n/a		

	Replacement/addition of a site where batch control/testing takes place A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)				
II/0011	Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to include new safety information about Extramedullary Hematopoietic Masses in transfusion-dependent β-thalassemia patients based on the open-label phase of the ACE-536-B-THAL-001 Phase III study, the long-term follow-up study and post marketing data. 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	26/01/2023	27/02/2023	SmPC and PL	New contraindication in patients requiring treatment to control the growth of EMH masses and new warning in section 4.4 of SmPC providing information based on the pivotal study and the long term follow-up study, on frequencies of occurrence of extramedullary haemopoiesis (EMH) masses and spinal cord compression symptoms due to EMH masses in transfusion-dependent □-thalassaemia patients. EMH has also been recorded as ADR as common for the □-thalassaemia indication in section 4.8 of the SmPC. Please refer to Scientific Discussion 'Reblozyl-H-C-4444-II-11' For more information, please refer to the Summary of Product Characteristics.
II/0009	Extension of indication in β-thalassaemia to include adult patients with non-transfusion dependent β-thalassaemia (NTDT) for Reblozyl; 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. Version 1.3 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.	26/01/2023	27/02/2023	SmPC and PL	Please refer to Scientific Discussion 'Reblozyl-H-C-4444-II-09'

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10860 /202206	Periodic Safety Update EU Single assessment - luspatercept	12/01/2023	n/a		PRAC Recommendation - maintenance
II/0013	B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	10/11/2022	n/a		
IB/0015	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	05/10/2022	n/a		
IB/0012	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	12/09/2022	27/02/2023	SmPC	
PSUSA/10860 /202112	Periodic Safety Update EU Single assessment - luspatercept	07/07/2022	n/a		PRAC Recommendation - maintenance
PSUSA/10860 /202106	Periodic Safety Update EU Single assessment - luspatercept	13/01/2022	n/a		PRAC Recommendation - maintenance
IAIN/0008/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release	31/08/2021	19/09/2022	SmPC, Annex II and PL	

	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 C.I.3.a - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Implementation of wording agreed by the competent authority				
IAIN/0006/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 A.7 - Administrative change - Deletion of manufacturing sites B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	22/07/2021	n/a		
PSUSA/10860 /202012	Periodic Safety Update EU Single assessment - luspatercept	08/07/2021	n/a		PRAC Recommendation - maintenance
IB/0005/G	This was an application for a group of variations. 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	26/05/2021	n/a		

	control/testing takes place				
T/0003	Transfer of Marketing Authorisation	20/01/2021	04/02/2021	SmPC, Labelling and PL	
II/0002/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes 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.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 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	10/12/2020	n/a		

II/0001/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological 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 B.I.b.2.z - Change in test procedure for AS or	26/11/2020	04/02/2021	Annex II	

	starting material/reagent/intermediate - Other variation				