ROCTAVIAN

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/11009 /202408	Periodic Safety Update EU Single assessment - valoctocogene roxaparvovec	13/03/2025	n/a		PRAC Recommendation - maintenance
II/0014	Update of the Annex II in order to implement changes the current marketing authorisation obligations for ROCTAVIAN. The RMP version 1.3 has	27/02/2025		Annex II	At the time of approval, the MAH committed to perform 2 long-term studies (270-601 and 270-801). Both studies are intended to better characterize the long-term effectiveness

[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).

	also been submitted. 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				and safety of Roctavian in patients in a real-world setting. As part of this variation the MAH expressed its intention to stop study 270-601 and to only monitor long term follow up of treated patients through the non-interventional study 270-801. Having in mind the overlap in the objectives of both studies and the critical challenge in maintaining both, CAT accepted the MAH's intention to rely only on data coming only from study 270-801. For more information, please refer to the Summary of Product Characteristics and Annex II.
IA/0015	A.7 - Administrative change - Deletion of manufacturing sites	08/10/2024	n/a		
PSUSA/11009 /202402	Periodic Safety Update EU Single assessment - valoctocogene roxaparvovec	03/10/2024	n/a		PRAC Recommendation - maintenance
IB/0013	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	29/08/2024	n/a		
R/0011	Renewal of the marketing authorisation.	27/06/2024	16/08/2024	SmPC	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for ROCTAVIAN, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.

II/0010	Submission of the final report from study BMN270-302 listed as a category 3 study in the RMP (phase 3 open-label, single-arm study to evaluate the efficacy and safety of BMN 270, an adeno-associated virus vector–mediated gene transfer of human factor VIII at a dose of 4x1013 vg/kg in hemophilia A patients with residual FVIII levels ≤ 1 IU/dL receiving prophylactic FVIII infusions). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/04/2024	n/a		The MAH has submitted the final results of the study BMN270-302: A phase 3 open label, single-arm study to evaluate the efficacy and safety of BMN 270, an adeno-associated virus vector–mediated gene transfer of human factor VIII at a dose of 4x1013 vg/kg in hemophilia A patients with residual FVIII levels ≤ 1 IU/dL receiving prophylactic exogenous FVIII infusions for a minimum of one year prior to enrolment. Only 1 participant was enrolled in 270-302. Efficacy data are in line with expectations, given the suboptimal dose received of 4x1013 vg/kg: patient returned to FVIII prophylaxis and then emicizumab. No new safety concerns has been raised from the study 270-302. Based on the results of this study, no updates are proposed to the Summary of Product Characteristics (SmPC). The benefit-risk balance of ROCTAVIAN, remains positive.
PSUSA/11009 /202308	Periodic Safety Update EU Single assessment - valoctocogene roxaparvovec	11/04/2024	n/a		PRAC Recommendation - maintenance
II/0008/G	This was an application for a group of variations. Grouped application comprising two variations as follows: C.I.4 - Update of section 4.5 of the SmPC in order to add drug-drug interaction information with Isotretinoin and Efavirenz based on results from study "In vitro Drug-Drug Interaction Study: Effects of Concomitant Administration of Isotretinoin, Amphetamine, Omeprazole, Celecoxib and Selected HAART Medications with AAV5-FVIII-SQ on	09/11/2023	16/08/2024	SmPC	SmPC section 4.5 new text: Isotretinoin (…) An in vitro study in human primary hepatocytes indicated that isotretinoin suppressed factor VIII expression independent of hepatotoxicity. Isotretinoin is not recommended in patients who are benefiting from valoctocogene roxaparvovec. Efavirenz An in vitro study in human primary hepatocytes indicated that efavirenz suppressed factor VIII expression

	Cytotoxicity and AAV5-FVIII-SQ DNA and RNA Expression in Primary Human Hepatocytes". A.6 - To change the ATC Code from B02BD15 to "not yet assigned". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data A.6 - Administrative change - Change in ATC Code/ATC Vet Code				independent of hepatotoxicity. Efavirenz is not recommended in patients who are benefiting from valoctocogene roxaparvovec. The use of non efavirenz treatments should be considered. For more information, please refer to the Summary of Product Characteristics.
PSUSA/11009 /202302	Periodic Safety Update EU Single assessment - valoctocogene roxaparvovec	28/09/2023	n/a		PRAC Recommendation - maintenance
IB/0007	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	08/09/2023	16/08/2024	SmPC	
IB/0006	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	23/08/2023	n/a		
R/0003	Renewal of the marketing authorisation.	25/05/2023	24/07/2023	SmPC	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for ROCTAVIAN, subject to

					the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0004/G	This was an application for a group of variations. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal 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	26/04/2023	n/a		
IB/0002	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	09/11/2022	24/07/2023	SmPC, Labelling and PL	
IB/0001	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	27/10/2022	n/a		