Mepsevii

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
IA/0040/G	This was an application for a group of variations. B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.d.2.a - Change in test procedure for the finished	26/06/2024		Annex II and PL	

[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).

	product - Minor changes to an approved test procedure A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites 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)				
PSUSA/10709 /202311	Periodic Safety Update EU Single assessment - vestronidase alfa	13/06/2024	n/a		PRAC Recommendation - maintenance
IB/0037	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	08/01/2024	n/a		
S/0036	Annual re-assessment.	09/11/2023	n/a		
IB/0035	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	22/09/2023	n/a		
R/0033	Renewal of the marketing authorisation.	25/05/2023	28/07/2023	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Mepsevii in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.

PSUSA/10709 /202211	Periodic Safety Update EU Single assessment - vestronidase alfa	08/06/2023	n/a		PRAC Recommendation - maintenance
S/0032	Annual re-assessment.	10/11/2022	n/a		
IB/0031	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	19/08/2022	n/a		
PSUSA/10709 /202111	Periodic Safety Update EU Single assessment - vestronidase alfa	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0030	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	03/05/2022	n/a		
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2021	28/07/2023	PL	
II/0024	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	02/12/2021	n/a		
IB/0027	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	25/11/2021	n/a		
IB/0026	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	25/11/2021	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
S/0025	Annual re-assessment.	11/11/2021	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Mepsevii should be maintained.
IB/0023/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	13/08/2021	n/a		
PSUSA/10709 /202011	Periodic Safety Update EU Single assessment - vestronidase alfa	10/06/2021	n/a		PRAC Recommendation - maintenance
II/0019	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	09/04/2021	n/a		
IA/0022	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	09/02/2021	n/a		
IB/0020	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	11/01/2021	n/a		

S/0017	Annual re-assessment.	10/12/2020	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Mepsevii should be maintained.
PSUSA/10709 /202005	Periodic Safety Update EU Single assessment - vestronidase alfa	26/11/2020	n/a		PRAC Recommendation - maintenance
IAIN/0018	A.1 - Administrative change - Change in the name and/or address of the MAH	24/09/2020	22/09/2021	SmPC, Labelling and PL	
IB/0016/G	This was an application for a group of variations. 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 B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	17/09/2020	n/a		
II/0013/G	This was an application for a group of variations. 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.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change	23/07/2020	n/a		

	to an approved stability protocol				
II/0014	Update of sections 4.4,4.8 and 5.1 of the SmPC following the assessment of final results from study UX003-CL202, a multicenter, multinational, open-label treatment, extension of study UX003-CL301 in subjects with MPS VII, previously submitted under Article 46 of Regulation (EC) No 1901/2006; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the Product Information. C.I.3.b - 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 - Change(s) with new additional data submitted by the MAH	16/07/2020	30/09/2020	SmPC and PL	Significant sustained reductions in urinary glycosaminoglycans (Dermatan Sulfate) were observed in patients with Mucopolysaccharidosis VII after treatment with vestronidase alfa of up to 3.6 years. Additional beneficial responses following long term treatment with vestronidase alfa was seen in some treated patients, including a sustained increase in the results of the 6-Minute Walk Test. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10709 /201911	Periodic Safety Update EU Single assessment - vestronidase alfa	11/06/2020	n/a		PRAC Recommendation - maintenance
IB/0011	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/03/2020	n/a		
II/0009	Update of sections 4.8. 5.1 and 5.2 of the SmPC following final results from paediatric study UX003-CL203, an open –label study of vestrodinase alfa enzyme replacement therapy in MPS 7 patients less than 5 years old.	23/01/2020	30/09/2020	SmPC	In an open-label, uncontrolled single arm study eight patients less than 5 years of age received a dose of 4 mg/kg vestronidase alfa every two weeks for 48 weeks of treatment period and additional up to 240 weeks during optional continuation period. Treatment with vestronidase alfa resulted in a rapid and

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				sustained, highly significant reduction in urinary glycosaminoglycans Dermatan Sulfate (uGAG DS) excretion with a mean percent change of -60% at Week 4 which was sustained at Week 48. Subjects who entered the Continuation Period up to Week 132 experienced further reduction in uGAG DS. A positive trend toward increased growth velocity was observed after vestronidase alfa treatment. All 3 subjects with hepatomegaly assessed by ultrasound examination at Baseline had decreased liver size to within normal range for age and sex prior to study termination.
PSUSA/10709 /201905	Periodic Safety Update EU Single assessment - vestronidase alfa	28/11/2019	n/a		PRAC Recommendation - maintenance
S/0007	Annual re-assessment.	14/11/2019	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Mepsevii should be maintained.
IAIN/0010	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	05/11/2019	n/a		
II/0008	Update of section 5.3 of the SmPC based on the final results from study UX003-PC010 a Developmental and Perinatal/Postnatal reproduction non-clinical study in rats including a Post-natal Behavioural/Functional Evaluation. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1.	17/10/2019	30/09/2020	SmPC	A pre-and postnatal development study in which rats were administered with UX003 once every three days beginning on Gestation Day 7 through Day 20 postpartum did not show an effect on clinical signs, growth and sexual maturation, neurobehavioral or reproductive function or any macroscopic observations in the F1 generation rats.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10709 /201811	Periodic Safety Update EU Single assessment - vestronidase alfa	14/06/2019	n/a		PRAC Recommendation - maintenance
IB/0005	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	13/06/2019	16/09/2019	SmPC, Labelling and PL	
IAIN/0004/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 A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.c.1 - Change to importer, batch release 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	08/04/2019	16/09/2019	Annex II and PL	
IB/0002/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 -	23/10/2018	n/a		

	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 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.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IAIN/0001/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.2.c.1 - Change to importer, batch release 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	27/09/2018	16/09/2019	Annex II and PL	