Galafold

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/10507 /201711	Periodic Safety Update EU Single assessment - migalastat	14/06/2018	n/a		PRAC Recommendation - maintenance
IB/0015	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/04/2018		SmPC	
IB/0013	A.z - Administrative change - Other variation	16/01/2018	12/04/2018	SmPC, Labelling 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).

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PSUSA/10507 /201705	Periodic Safety Update EU Single assessment - migalastat	11/01/2018	n/a		PRAC Recommendation - maintenance
II/0011	Update of section 4.2 of the SmPC to provide further information on missing doses and to improve wording on the administration with food. No new data is submitted to support these changes. In addition, the MAH took this opportunity to include the ATC code and to update the local representatives in the Package Leaflet. Consequently changes are proposed in Annex I, IIIA and IIIB. The RMP version 2.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/10/2017	12/04/2018	SmPC, Labelling and PL	
II/0010	Update of section 5.1 of the SmPC to reflect the final results from study AT1001-041: A phase 3 open label extension study to assess the safety and efficacy of 150 mg migalastat HCl QOD in subjects with Fabry disease who have completed Studies AT1001-011, AT1001- 012 or FAB-CL-205, listed as a category 3 study in the RMP. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/10/2017	12/04/2018	SmPC	
PSUSA/10507	Periodic Safety Update EU Single assessment -	09/06/2017	n/a		PRAC Recommendation - maintenance

/201611	migalastat				
II/0009	Update of section 5.1 of the SmPC to add new mutations in Table 2: Galafold (migalastat) amenability table and to Table 3: Mutations not amenable to Galafold (migalastat). In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some minor editorial changes to the tables and to update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/05/2017	12/04/2018	SmPC and PL	
II/0005	B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP	06/04/2017	n/a		
IA/0007	B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	17/02/2017	n/a		
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	07/02/2017	n/a		
II/0002	Update of section 5.1 of the SmPC namely the mutations tables to reflect to 66 newly tested	13/10/2016	12/04/2018	SmPC	Using the validated human embryonic kidney (HEK) assay to assess/predict whether a GLA mutation is responsive to

	mutations that are either amenable or non-amenable to migalastat. The MAH also took this opportunity to introduced minor editorial changes in the tables. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				migalastat, the MAH tested 66 mutations upon physician's request and/or new mutations from literature. For each mutation the MAH submitted an analytical study report, confirming whether the tested mutations are amenable or non-amenable to migalastat. As a result of this variation, section 5.1 of the SmPC is being updated to include 66 newly tested mutations, 15 mutations that did not qualify for testing.
II/0001	Update of sections 4.8 and 5.1 of the SmPC to reflect the 30 month data results of study AT1001-012: an active-controlled, randomised, open-label comparing the efficacy and safety of migalastat to enzyme replacement therapy (ERT) in patients with Fabry disease who were receiving ERT prior to study entry and who had a migalastat-responsive GLA mutation. This variation fulfils a post approval commitment Cat 3:01 as defined in the risk management plan. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and to update the contact details of some local representatives in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/10/2016	12/04/2018	SmPC and PL	The final 30 month data results of study AT1001-012: an active-controlled, randomised, open-label comparing the efficacy and safety of migalastat to enzyme replacement therapy (ERT) in patients with Fabry disease who were receiving ERT prior to study entry and who had a migalastat-responsive GLA mutation were submitted in this variation. These data showed a similar consistent trend on eGFR and LVMi/LVH under continued treatment with migalastat, as seen during the first 18 months of the study. All other secondary endpoints follow a similar trend. Therefore, based on the submitted data no new or unexpected efficacy findings were observed apart from a 10% increase in renal events that warrants follow up information. Section 5.1 of the SmPC reflects these results. These 30 months data did not result in unexpected safety findings. The adverse events (AEs) reported were in line for what was reported in the 18 months comparative part of the study. Based on the overall commonly reported AEs "pain in the extremity" and "pain (general)" were added to section 4.8 of the SmPC.
IB/0003	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	19/09/2016	12/04/2018	SmPC	
