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
IA/0039	B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	24/05/2023	n/a		
II/0038	Please refer to the Recommendations section C.I.4 - Change(s) in the SPC, Labelling or PL due to	26/04/2023		SmPC, Labelling and	Galafold exposure is decreased by approximately 40% when taken with food and 60% when taken with coffee. Food and caffeine should not be consumed at least 2 hours

[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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	new quality, preclinical, clinical or pharmacovigilance data			PL	before and 2 hours after taking Galafold to give a minimum 4 hours fast. Water (plain, flavored, sweetened), fruit juices without pulp, and caffeine-free carbonated beverages can be consumed during the 4-hour fasting period.
IB/0037	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/05/2022	15/03/2023	SmPC and PL	Update of Section 5.1 of the SmPC by adding new amenable mutations.
PSUSA/10507 /202105	Periodic Safety Update EU Single assessment - migalastat	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0034	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/01/2022	15/03/2023	SmPC and PL	
IA/0036/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting	22/12/2021	n/a		

	material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material) B.III.1.b.4 - Submission of a new/updated or				

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II/0029	Extension of indication for Galafold (migalastat) to include long-term treatment of adolescents 12 to < 16 years with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.2 of the SmPC and Section 1 and 2 of the Package Leaflet are updated accordingly. A revised RMP version 6 has also been submitted. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	24/06/2021	23/07/2021	SmPC and PL	Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-0029'
IAIN/0033	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same	24/06/2021	n/a		

	pharmaceutical group as the currently approved manufacturer				
IA/0032	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	25/05/2021	n/a		
IAIN/0031	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	11/05/2021	n/a		
II/0030	Update Section 5.1 of the SmPC based on final results from study AT1001-042 listed as category 3 in the RMP. Study AT1001-042-is an open-label, non-comparative, long-term extension study to evaluate long term safety and efficacy of migalastat l monotherapy in subjects with Fabry disease. The updated RMP version 5.1 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/03/2021	23/07/2021	SmPC	Results from study AT1001-042, including 84 patients, suggested that under continued migalastat treatment in adults, the disease symptoms (particularly renal and cardiac outcomes) improve and remain stable. For more information, please refer to the Summary of Product Characteristics.
R/0027	Renewal of the marketing authorisation.	10/12/2020	11/02/2021	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 Galafold in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.

PSUSA/10507 /202005	Periodic Safety Update EU Single assessment - migalastat	14/01/2021	n/a		PRAC Recommendation - maintenance
II/0025	Update to the Galafold Summary of Product Characteristics (SmPC), Section 5.1 Pharmacodynamic Properties to add 1017 new amenable mutations in Table 2: Galafold (migalastat) amenability table and delete the entire Table 3: Mutations not amenable to Galafold (migalastat). In addition, the MAH took the opportunity to update contact details of the MAH and Belgium local representatives and the Labelling (outer packaging), Section 5. Method and Route(s) of administration as well as Package Leaflet, Section 3. How to take Galafold in order to improve the instructions for opening and removal of the capsules out of the packaging. Editorial linguistic changes are made in Czech, Dutch, Finnish, Greek, Polish, Icelandic, Italian and Swedish languages. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/05/2020	11/02/2021	SmPC, Labelling and PL	Update to include 1017 newly tested mutations that are amenable to migalastat and deletion of non-amenable mutations to balance the SmPC information for the prescribers, since the website www.Galafoldamenabilitytable.com is also included in the SmPC and always contains the list of non-amenable mutations. In addition, improvements in the instructions for opening and removal of the capsules out of the packaging following a user testing results.
IA/0026	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	11/05/2020	n/a		
PSUSA/10507	Periodic Safety Update EU Single assessment -	16/01/2020	n/a		PRAC Recommendation - maintenance

/201905	migalastat				
PSUSA/10507 /201811	Periodic Safety Update EU Single assessment - migalastat	14/06/2019	n/a		PRAC Recommendation - maintenance
IA/0023/G	This was an application for a group of variations. 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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	31/05/2019	n/a		
IA/0022	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	30/04/2019	n/a		
IA/0021	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	30/04/2019	n/a		
T/0020	Transfer of Marketing Authorisation	19/03/2019	28/03/2019	SmPC, Labelling and PL	
IAIN/0018	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	25/02/2019	28/03/2019	Annex II and	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing			PL	
PSUSA/10507 /201805	Periodic Safety Update EU Single assessment - migalastat	17/01/2019	n/a		PRAC Recommendation - maintenance
IB/0017	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/10/2018	28/03/2019	SmPC, Labelling and PL	
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	28/03/2019	SmPC	
IB/0013	A.z - Administrative change - Other variation	16/01/2018	12/04/2018	SmPC, Labelling and PL	
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	26/10/2017	12/04/2018	SmPC, Labelling and PL	

	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				
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 /201611	Periodic Safety Update EU Single assessment - migalastat	09/06/2017	n/a		PRAC Recommendation - maintenance
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	11/05/2017	12/04/2018	SmPC and PL	

	new quality, preclinical, clinical or pharmacovigilance data				
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 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	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 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	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

	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				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	