Grastofil

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
IB/0026	B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation	10/10/2018	n/a		
R/0020	Renewal of the marketing authorisation.	26/07/2018	04/10/2018	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Grastofil 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).

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IB/0024/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 B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	17/09/2018	n/a		
IB/0023/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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	24/08/2018	n/a		
IB/0025	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a	10/08/2018	n/a		

	biological/immunological AS is increased/decreased without process change (e.g. duplication of line)				
IB/0022/G	This was an application for a group of variations. B.I.b.z - Change in control of the AS - Other variation B.I.b.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to OCABR 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 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 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.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with	06/07/2018	n/a		

	its corresponding test method				
IB/0021/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	26/06/2018	30/07/2018	SmPC and PL	
IB/0018	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/09/2017	n/a		
IAIN/0019	A.1 - Administrative change - Change in the name and/or address of the MAH	18/08/2017	30/07/2018	SmPC, Labelling and PL	
IB/0017	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	07/07/2017	n/a		
IA/0016	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)	29/06/2017	n/a		
IAIN/0015	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	07/04/2017	n/a		

	site				
IB/0014	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	04/01/2017	n/a		
IAIN/0013	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	03/10/2016	n/a		
IB/0012/G	This was an application for a group of variations. C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference	01/08/2016	26/06/2017	SmPC, Labelling and PL	

	product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH				
PSUSA/1391/ 201509	Periodic Safety Update EU Single assessment - filgrastim	13/05/2016	n/a		PRAC Recommendation - maintenance
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/01/2016	26/06/2017	PL	
IB/0009/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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	05/01/2016	n/a		

IB/0008	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	11/08/2015	08/09/2015	SmPC and PL	
II/0007	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	20/11/2014	n/a		
IB/0006	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	22/10/2014	08/09/2015	SmPC and PL	
IB/0005	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	22/10/2014	08/09/2015	SmPC and PL	
II/0003/G	This was an application for a group of variations. Update the product information to include the paediatric population in the currently approved indication for use in adults, as per the reference product SmPC, and to introduce graduations on the syringe barrel enabling use of the Grastofil in accordance with the paediatric posology. Sections 4.1, 4.2, 4.8 and 6.5 of the SmPC and Section 3 and 6 of the Package Leaflet have been updated with the	25/04/2014	22/05/2014	SmPC and PL	The MAH submitted a group of variations to introduce minor graduations in the existing prefilled syringe for both strengths in order to include the paediatric population in the currently approved indication, as per the reference product SmPC, The MAH conducted two dose accuracy studies, one study evaluating 0.1, 0.2, 0.3 and 0.4 mL graduations and the second study evaluating minor gradations at increments of 0.025 mL. The results from the second study confirm a similar level of error margin as seen in the initial study. The data demonstrate that higher variances are not evident at

	paediatric use. In addition, Sections 5.1 and 6.6 of the SmPC have been updated in alignment with the Neupogen PI. C.I.2.b - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Change(s) require to be further substantiated by new additional data to be submitted by the MAH B.II.e.6.z - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Other variation				the 0.025 mL graduations relative to the 0.1 mL graduations. The product information has been updated in alignment with the Neupogen PI. The benefit risk of Grastofil use in the paediatric population is considered positive.
IB/0004	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	14/02/2014	22/05/2014	SmPC	
IB/0002	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	17/12/2013	22/05/2014	SmPC and PL	
IA/0001/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	26/11/2013	22/05/2014	Annex II	

	manufacturer of a novel excipient 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)				