EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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/0043	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	24/08/2023		SmPC 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).

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IB/0042/G	This was an application for a group of variations. 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 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	23/06/2023	n/a		
IA/0041/G	This was an application for a group of variations. B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	25/01/2023	n/a		
PSUSA/1391/ 202109	Periodic Safety Update EU Single assessment - filgrastim	05/05/2022	n/a		PRAC Recommendation - maintenance

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IB/0040/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	12/04/2022	n/a		
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2021		PL	
IB/0037	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	19/11/2020	n/a		
IB/0036	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	30/09/2020	n/a		
IAIN/0035	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	29/09/2020	23/09/2021	Annex II and PL	

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	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing				
IB/0034/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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	18/09/2020	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/09/2020	23/09/2021	PL	
IB/0033/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.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion	21/07/2020	n/a		

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	of a non-significant in-process test				
II/0030	Submission of an updated RMP version 6.0 in order to update the safety concerns and section of additional pharmacovigilance activities (removal of SCNIR and EBMT registry) in-line with latest approved Accofil (Filgrastim) RMP v4.0, dated 25-Jun-2019 approved on 03-Oct-2019 with procedure EMEA/H/C/003956/II/0037 as per the transfer of Marketing Authorisation of Grastofil from Apotex Netherland B.V to Accord healthcare S.L.U. Spain, for Grastofil 30 MU/0.5 ml & 48 MU/0.5 ml solution for injection or infusion in pre-filled syringe. 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	11/06/2020	n/a		
II/0031/G	This was an application for a group of variations. 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.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol	28/05/2020	n/a		

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	product and any of the test methods at the site is a biol/immunol method 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 B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)				
II/0029	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	28/05/2020	n/a		
T/0028	Transfer of Marketing Authorisation	18/11/2019	09/12/2019	SmPC, Labelling and PL	
PSUSA/1391/ 201809	Periodic Safety Update EU Single assessment - filgrastim	16/05/2019	n/a		PRAC Recommendation - maintenance
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	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

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				PL	therefore recommended the renewal of the marketing authorisation with unlimited validity.
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	24/08/2018	n/a		

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	and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0025	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	10/08/2018	n/a		
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	06/07/2018	n/a		

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	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 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		

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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 site	07/04/2017	n/a		
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	01/08/2016	26/06/2017	SmPC, Labelling and PL	

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	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 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	

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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	

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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 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	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 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	17/12/2013	22/05/2014	SmPC and PL	

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	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				
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 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)	26/11/2013	22/05/2014	Annex II	

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