Plegridy

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
N/0079	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/01/2025		PL	
IA/0077/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of	08/10/2024	n/a		

[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).

	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)				
IB/0076	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	29/04/2024	n/a		
IB/0075	B.I.b.z - Change in control of the AS - Other variation	06/11/2023	n/a		
IB/0073	B.II.c.z - Change in control of excipients in the Finished Product - Other variation	08/09/2023	n/a		
II/0070	Submission of the final report from study 105MS401. The objective of this study was to determine the incidence of serious adverse events (SAEs) in patients with relapsing forms of MS in routine clinical practice and to assess the overall long-term clinical effectiveness of peginterferon beta-1a in patients with relapsing forms of MS in routine clinical practice. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	31/08/2023	n/a		N/A
IB/0072	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	18/08/2023	n/a		

IA/0074	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	10/08/2023	n/a		
IA/0071/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.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	07/08/2023	n/a		
II/0068	Update of section 4.6 of the SmPC in order to update the information relating to secretion in human milk based on the results from study US-PEG-15-10936, a prospective, open label, post marketing study that measured Plegridy concentrations in breast milk in 6 lactating patients with Multiple Sclerosis. In addition, the MAH took the opportunity 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	30/03/2023	19/03/2024	SmPC and PL	The SmPC section 4.6 has been updated regarding breast-feeding since information available overall suggests that levels of interferon beta-1a/peginterferon beta-1a excreted in human milk are negligible and no harmful effects on the breastfed newborn/infant are anticipated. The PL has been updated accordingly. For more information, please refer to the Summary of Product Characteristics.

IA/0069	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	20/01/2023	n/a		
II/0067	B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	07/07/2022	n/a		
PSUSA/10275 /202107	Periodic Safety Update EU Single assessment - peginterferon beta-1A	10/02/2022	n/a		PRAC Recommendation - maintenance
IB/0064	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	21/10/2021	n/a		
IA/0065	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/10/2021	n/a		
IA/0063	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)	25/03/2021	n/a		
IAIN/0062/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	11/02/2021	04/02/2022	Annex II and PL	

	manufacturer of a novel excipient A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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				
PSUSA/10275 /202007	Periodic Safety Update EU Single assessment - peginterferon beta-1A	11/02/2021	n/a		PRAC Recommendation - maintenance
IA/0061	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/02/2021	n/a		
X/0056	Annex I_2.(e) Change or addition of a new route of administration	15/10/2020	14/12/2020	SmPC, Labelling and PL	
IA/0060/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	09/12/2020	n/a		
N/0058	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/08/2020	24/09/2020	PL	

IA/0057	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	08/05/2020	n/a		
PSUSA/10275 /201907	Periodic Safety Update EU Single assessment - peginterferon beta-1A	13/02/2020	n/a		PRAC Recommendation - maintenance
II/0052/G	This was an application for a group of variations. To update sections 4.3 and 4.6 of the SmPC in order to remove the contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 of the SmPC. The Package leaflet has been updated accordingly. This submission fulfils MEA 8.2 and 002. The RMP has been updated (ver 4.3) to include changes to the safety specification related to Pregnancy missing information status, in light of the new safety information received, as well as updates to other key sections of the RMP, adapting to the requirements of the GVP Module 5 revision 2 guidelines. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	19/09/2019	24/09/2020	SmPC and PL	The SmPC section 4.3 has been updated to remove the contraindication 'initiation of treatment in pregnancy'. The SmPC section 4.6 has been updated as follows: Pregnancy A large amount of data (more than 1000 pregnancy outcomes) from registries and post-marketing experience indicates no increased risk of major congenital anomalies after pre-conception exposure to interferon beta or such exposure during the first trimester of pregnancy. However, the duration of exposure during the first trimester is uncertain, because data were collected when interferon beta use was contraindicated during pregnancy, and treatment likely interrupted when pregnancy was detected and/or confirmed. Experience with exposure during the second and third trimester is very limited. Based on animal data (see section 5.3), there is a possibly increased risk for spontaneous abortion. The risk of spontaneous abortions in pregnant women exposed to interferon beta cannot adequately be evaluated based on the currently available data, but the data do not suggest an

	data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				increased risk so far. If clinically needed, the use of Plegridy may be considered during pregnancy. Breast-feeding It is not known whether peginferferon beta-1a is secreted in human milk. Limited information available on the transfer of interferon beta-1a into breast milk, together with the chemical / physiological characteristics of interferon beta, suggests that levels of interferon beta-1a excreted in human milk are negligible. No harmful effects on the breastfed newborn/infant are anticipated. Plegridy can be used during breast-feeding. The PL has been updated accordingly.
IB/0054	B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation	30/04/2019	n/a		
R/0051	Renewal of the marketing authorisation.	31/01/2019	25/03/2019	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Plegridy in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10275 /201807	Periodic Safety Update EU Single assessment - peginterferon beta-1A	14/02/2019	n/a		PRAC Recommendation - maintenance

IB/0053/G	This was an application for a group of variations. 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 pharmaceutical group as the currently approved manufacturer B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material	13/02/2019	n/a		
II/0046	Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. RMP version 3.3 was also approved. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	04/10/2018	25/03/2019	SmPC	Review of available evidence supports the possibility of a causal relationship between use of peginterferon beta-1a and anaphylactic reaction. Sections 4.4 and 4.8 of the SmPC were updated to include information on anaphylaxis. The SmPC section 4.4 has been updated to include reference to cases of anaphylaxis, to read as follows: Serious hypersensitivity reactions including cases of anaphylaxis have been reported as a rare complication of treatment with interferon beta, including Plegridy. Patients should be advised to discontinue Plegridy and seek immediate medical care if they experience signs and symptoms of anaphylaxis or severe hypersensitivity. Treatment with Plegridy should not be restarted. Section 4.8 of the SmPC, under 'Hypersensitivity reactions' now mentions that in post marketing experience, serious hypersensitivity events including cases of anaphylaxis have

					been reported (with frequency not known) following Plegridy administration.
IB/0048	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	24/08/2018	n/a		
T/0049	Transfer of Marketing Authorisation	03/07/2018	19/07/2018	SmPC, Labelling and PL	
IB/0047	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	14/06/2018	n/a		
N/0045	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/04/2018	19/07/2018	Labelling and PL	
IB/0044	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	08/03/2018	n/a		
II/0040	To add an alternate pre-filled syringe (Neopak). The components´ materials of the finished product container closure system of the existing pre-filled syringe (Hypak) and the new pre-filled syringe are identical. B.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is	22/02/2018	n/a		

	an integrated part of the primary packaging				
PSUSA/10275 /201707	Periodic Safety Update EU Single assessment - peginterferon beta-1A	08/02/2018	n/a		PRAC Recommendation - maintenance
IB/0043	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	10/01/2018	n/a		
IB/0042	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	06/12/2017	n/a		
IA/0041	A.7 - Administrative change - Deletion of manufacturing sites	17/11/2017	n/a		
PSUSA/10275 /201701	Periodic Safety Update EU Single assessment - peginterferon beta-1A	14/09/2017	10/11/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10275/201701.
IB/0037/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	13/10/2017	n/a		
IAIN/0038/G	This was an application for a group of variations.	08/09/2017	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IB/0036	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/05/2017	10/11/2017	Annex II and Labelling	
IB/0034	A.7 - Administrative change - Deletion of manufacturing sites	26/04/2017	n/a		
PSUSA/10275 /201607	Periodic Safety Update EU Single assessment - peginterferon beta-1A	09/02/2017	n/a		PRAC Recommendation - maintenance
IA/0033	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	16/12/2016	n/a		
IA/0032	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	16/12/2016	n/a		
II/0031/G	This was an application for a group of variations. II: C.I.4 Update of section 4.8 of the SmPC with data on exposure and section 5.1 of the SmPC with information on maintenance of long-term efficacy based on clinical study data (study ATTAIN) II: C.I.4 Update of section 4.8 of the SmPC in order to add information concerning the onset and duration of flu-like symptoms based on clinical study data (study ALLOW). The Package Leaflet is updated	15/12/2016	10/11/2017	SmPC and PL	In view of the new emerging data from two clinical studies, the Product Information was updated with regards to efficacy, safety and tolerability of the product. The following revisions were introduced in section 4 of the Package Leaflet to add information on managing flu-like symptoms (new text bold, old text in strikethrough mode): Three simple ways to help reduce the impact of flu-like symptoms:

	accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				1. (Strikethrough text) Use your Plegridy injection just before bedtime. This may allow you to sleep through the effects. (To be replaced with the following text) Consider the timing of your Plegridy injection. The start and end of flu-like symptoms are different for every patient. On average, flu-like symptoms begin approximately 10 hours after injection and last between 12 and 24 hours. 2. Take paracetamol or ibuprofen half an hour before your Plegridy injection. (Strikethrough text) and continue taking it for up to a day. Speak to your doctor or pharmacist about (To be replaced with the following text) how much to take and how long to take it. (Strikethrough text) the right dose. 3. If you have a fever, drink plenty of water to keep you hydrated.
II/0027	Introduction of real-time release testing of the pre-filled pen presentations. B.II.d.3 - Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product	15/09/2016	n/a		
IB/0029	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	12/09/2016	n/a		
PSUSA/10275 /201601	Periodic Safety Update EU Single assessment - peginterferon beta-1A	02/09/2016	n/a		PRAC Recommendation - maintenance
WS/0927	This was an application for a variation following a worksharing procedure according to Article 20 of	14/07/2016	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol				
N/0028	Update of the package leaflet with revised contact details of the local representatives for Romania and Norway. In addition the MAH took the opportunity to make minor linguistic amendments to the French Labelling and Finnish package leaflet and instructions for use. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/06/2016	08/09/2016	PL	
IB/0024	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	05/04/2016	n/a		
N/0023	Update of the Package Leaflet with revised contact details of the local representatives for Estonia and Latvia and formatting changes were made to the Package Leaflet in line with the user testing. In addition, the MAH took the opportunity to make minor linguistic amendments , formatting changes and alignments of texts to ensure consistency in the Labelling and Package Leaflets for: EN, CS, DE, ES, FI, HR, IT, PT, RO, SL, and SE.	11/02/2016	08/09/2016	PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
PSUSA/10275 /201507	Periodic Safety Update EU Single assessment - peginterferon beta-1A	11/02/2016	n/a		PRAC Recommendation - maintenance
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/12/2015	08/09/2016	PL	
IB/0021	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	13/11/2015	n/a		
WS/0805	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC section 4.8 and PL section 4 in order to include class text for interferon-beta products regarding pulmonary arterial hypertension (PAH). This change has been agreed by PRAC and endorsed by CHMP on 23 April 2015. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/10/2015	08/09/2016	SmPC and PL	
WS/0806	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of SmPC, Labelling and Package Leaflet in line with EMA recommendation and QRD template. In addition, MAH took the opportunity to implement	17/09/2015	08/09/2016	SmPC, Labelling and PL	

	linguistic and editorial corrections. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IG/0615	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	11/09/2015	n/a		
PSUSA/10275 /201501	Periodic Safety Update EU Single assessment - peginterferon beta-1A	10/09/2015	n/a		PRAC Recommendation - maintenance
IA/0017	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	07/08/2015	n/a		
WS/0750	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	06/08/2015	n/a		
IA/0016	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	30/07/2015	n/a		

IB/0014/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	28/07/2015	n/a		
IB/0012	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	27/07/2015	n/a		
IA/0011/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.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former	01/07/2015	n/a		

	non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material				
IAIN/0010	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	26/06/2015	08/09/2015	Annex II and PL	
IB/0008/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	23/06/2015	n/a		
IG/0558/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	12/05/2015	n/a		

	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)				
II/0004/G	This was an application for a group of variations. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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	22/01/2015	08/09/2015	Annex II	
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/10/2014	08/09/2015	PL	
IB/0001/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.d.2.a - Change in test procedure for the finished	11/09/2014	n/a		

	product - Minor changes to an approved test procedure				
IB/0002	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	09/09/2014	08/09/2015	SmPC	
IB/0003/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 B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	03/09/2014	n/a		