Alprolix

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
IAIN/0047	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	06/11/2024		Annex II 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).

IB/0046/G	This was an application for a group of variations. B.II.d.2.e - Change in test procedure for the finished product - Update of the test procedure to comply with the updated general monograph in the Ph. Eur. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	05/11/2024	n/a		
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/10/2024	n/a		
IB/0045	B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation	01/10/2024	n/a		
IB/0044/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.I.a.z - Change in 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	26/09/2024	n/a		
PSUSA/10499 /202303	Periodic Safety Update EU Single assessment - eftrenonacog alfa	09/11/2023	05/01/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10499/202303.
IB/0042/G	This was an application for a group of variations.	24/10/2023	n/a		

	B.II.d.2.z - Change in test procedure for the finished product - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation				
IA/0040/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.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	18/11/2022	n/a		
IB/0039	B.I.c.1.z - Change in immediate packaging of the AS - Other variation	31/01/2022	n/a		
IB/0038	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	03/12/2021	n/a		
II/0036/G	This was an application for a group of variations. B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test	09/09/2021	14/10/2022	Annex II	

	method at the site is a biol/immunol method 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.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
IA/0037	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)	17/05/2021	n/a		
R/0032	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 Alprolix in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0035	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	18/12/2020	n/a		

	material/intermediate				
IB/0034	B.II.z - Quality change - Finished product - Other variation	28/10/2020	n/a		
IB/0033	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	28/10/2020	n/a		
II/0029	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	03/09/2020	19/10/2020	SmPC and PL	Update of sections 4.2, 4.8 and 5.1 of the SmPC as well as PL section 4 to include paediatric data on Previously Untreated Patients (PUPs) following the completion of a phase III study 998HB303.
PSUSA/10499 /202003	Periodic Safety Update EU Single assessment - eftrenonacog alfa	01/10/2020	n/a		PRAC Recommendation - maintenance
IB/0031	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	13/07/2020	n/a		
II/0028	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	12/03/2020	n/a		
II/0026	B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for	12/12/2019	n/a		

	biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes				
PSUSA/10499 /201903	Periodic Safety Update EU Single assessment - eftrenonacog alfa	03/10/2019	n/a		PRAC Recommendation - maintenance
IAIN/0027	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	26/08/2019	n/a		
IB/0024	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	08/05/2019	n/a		
PSUSA/10499 /201809	Periodic Safety Update EU Single assessment - eftrenonacog alfa	11/04/2019	n/a		PRAC Recommendation - maintenance
II/0021	Update of sections 4.8 and 5.1 of the SmPC to include new clinical efficacy and safety data on long-term treatment with Alprolix. The submission includes integrated evaluation of data from the extension study 9HB01EXT (BYOND) which was submitted in a previous P46 procedure and the pivotal parent studies. The PL is updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest version of the "Excipients in the labelling and package leaflet of medicinal products for human use"guideline. The list of local representatives has	21/02/2019	11/02/2020	SmPC, Labelling and PL	

	been updated and other minor editorial changes have been included in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IA/0023	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)	17/01/2019	n/a		
II/0020	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 product and any of the test methods at the site is a biol/immunol method	22/11/2018	n/a		
PSUSA/10499 /201803	Periodic Safety Update EU Single assessment - eftrenonacog alfa	04/10/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10499 /201709	Periodic Safety Update EU Single assessment - eftrenonacog alfa	26/04/2018	06/07/2018	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10499/201709.
IA/0018	A.7 - Administrative change - Deletion of manufacturing sites	18/04/2018	n/a		
IB/0017	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	21/03/2018	n/a		

IB/0016	B.I.b.1.i - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Where there is no monograph in the European/National Ph. for the AS, a change in specification from in-house to a non-official/third country Ph.	15/03/2018	n/a		
IB/0015	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	05/03/2018	n/a		
IB/0014	B.II.z - Quality change - Finished product - Other variation	23/01/2018	n/a		
IB/0012	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)	15/12/2017	n/a		
PSUSA/10499 /201703	Periodic Safety Update EU Single assessment - eftrenonacog alfa	28/09/2017	n/a		PRAC Recommendation - maintenance
IA/0010	A.7 - Administrative change - Deletion of manufacturing sites	20/07/2017	n/a		
II/0006/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	20/07/2017	n/a		

	of the AS 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 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 B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation 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.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability				
IB/0009	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	20/06/2017	n/a		
IB/0007	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/06/2017	07/06/2018	SmPC, Labelling and	

				PL	
PSUSA/10499 /201609	Periodic Safety Update EU Single assessment - eftrenonacog alfa	20/04/2017	23/06/2017		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10499/201609.
IB/0002	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	14/12/2016	n/a		
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/10/2016	23/06/2017	Labelling	
IAIN/0003	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	17/10/2016	n/a		
T/0001	Transfer of marketing authorisation from Biogen Idec Ltd to Swedish Orphan Biovitrum AB (publ). Transfer of Marketing Authorisation	25/08/2016	30/09/2016	SmPC, Labelling and PL	