Beovu

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/0027/G	This was an application for a group of variations. 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 -	22/02/2024		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).

	Not including batch control/testing B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site A.7 - Administrative change - Deletion of manufacturing sites				
IA/0025	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	11/09/2023		Annex II	
II/0021	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/05/2023	29/06/2023	SmPC and PL	
II/0018	Update of sections 4.2 and 5.1 of the SmPC in order to introduce an alternative loading posology regimen for wet AMD and update information based on modelling and simulation studies; the Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/05/2023	29/06/2023	SmPC and PL	In treatment initiation, alternative loading dose regimen is 6 mg brolucizumab (0.05 ml solution) administered every 6 weeks for the first 2 doses, with a disease activity assessment suggested 12 weeks (3 months) after treatment start. A third dose may be administered based on disease activity as assessed by visual acuity and/or anatomical parameters at week 12. For more information, please refer to the Summary of Product Characteristics.

PSUSA/10829 /202210	Periodic Safety Update EU Single assessment - brolucizumab	12/05/2023	n/a		PRAC Recommendation - maintenance
IAIN/0024/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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.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.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	11/04/2023	29/06/2023	Annex II and PL	
IB/0023	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	20/02/2023	n/a		
IB/0020	B.II.z - Quality change - Finished product - Other variation	19/12/2022	n/a		

II/0019	B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	15/12/2022	29/06/2023	Annex II	
PSUSA/10829 /202204	Periodic Safety Update EU Single assessment - brolucizumab	27/10/2022	n/a		PRAC Recommendation - maintenance
IB/0017	B.II.z - Quality change - Finished product - Other variation	16/08/2022	n/a		
IA/0016	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	04/07/2022	n/a		
IG/1521	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	23/06/2022	n/a		
IB/0013	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	24/05/2022	n/a		
PSUSA/10829 /202110	Periodic Safety Update EU Single assessment - brolucizumab	05/05/2022	n/a		PRAC Recommendation - maintenance
II/0010	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	24/02/2022	28/03/2022	SmPC and PL	

II/0008	Update of Section 4.4 of the SmPC with a subsection on intraocular inflammation and update of the warning on intraocular inflammation including retinal vasculitis and/or retinal vascular occlusion, and update of Section 4.8 of the SmPC to update the frequency of the ADRs "Retinal vasculitis" and "Retinal vascular occlusion" to "uncommon"; to merge "Retinal artery occlusion" and "retinal vascular occlusion" into "retinal vascular occlusion"; and to update the description of immunogenicity. All of this is based on the final results of 2 retrospective real world studies that evaluated patients with nAMD for up to 6 months after initiating treatment with brolucizumab and a mechanistic study BASICHR0049 that identified an immune cause of intraocular inflammation including retinal vasculitis and retinal vascular occlusion. The Package Leaflet is updated accordingly. The updated RMP version 7.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/10/2021	18/11/2021	SmPC and PL	A higher number of intraocular inflammation events were observed among patients with treatment-emergent antibodies. After investigation, retinal vasculitis and/or retinal vascular occlusion were found to be immune mediated events. Intraocular inflammation, including retinal vasculitis and/or retinal vascular occlusion, may occur following the first intravitreal injection and at any time of treatment. These events were observed more frequently at the beginning of the treatment. Based on clinical studies, these events were more frequent in female patients treated with Beovu than male patients (e.g. 5.3% females vs. 3.2% males in HAWK and HARRIER) and in Japanese patients. Patients treated with Beovu with a medical history of intraocular inflammation and/or retinal vascular occlusion (within 12 months prior to the first brolucizumab injection) should be closely monitored, since they are at increased risk of developing retinal vasculitis and/or retinal vascular occlusion. For more information, please refer to the Summary of Product Characteristics.
II/0006	Update of section 4.2 of the SmPC to update the wording of the posology, following the assessment of procedure EMEA/H/C/004913/II/0002. In addition, section 4.4 of the SmPC is updated to inform that the interval between two Beovu doses during maintenance treatment should not be less than every	14/10/2021	18/11/2021	SmPC and PL	The interval between two Beovu doses during maintenance treatment should not be less than 8 weeks considering that a higher incidence of intraocular inflammation (including retinal vasculitis) and retinal vascular occlusion was reported in patients with nAMD who received Beovu every 4 week maintenance dosing in a clinical study compared to

	8 weeks as warranted and the Package Leaflet is updated accordingly. Furthermore, the marketing authorisation holder has taken the opportunity to implement minor editorial changes in section 6.5 of the SmPC. Furthermore, the CHMP considers that this variation implements changes to the decision granting the marketing authorisation due to a significant public health concern. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				patients who received Beovu every 8 or 12 week maintenance dosing in the pivotal Phase III clinical studies. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10829 /202104	Periodic Safety Update EU Single assessment - brolucizumab	28/10/2021	n/a		PRAC Recommendation - maintenance
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/09/2021	18/11/2021	PL	
PSUSA/10829 /202010	Periodic Safety Update EU Single assessment - brolucizumab	06/05/2021	n/a		PRAC Recommendation - maintenance
II/0005/G	This was an application for a group of variations. In view of the data submitted with the group of variations, amendments to Annex(es) II are recommended. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder	14/01/2021	19/07/2021	Annex II	

	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.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.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 B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
PSUSA/10829 /202004	Periodic Safety Update EU Single assessment - brolucizumab	29/10/2020	n/a		PRAC Recommendation - maintenance
II/0002	C.I.4, Update of sections 4. 4, and 4.8 of the SmPC in order to add a new warning on Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	03/09/2020	19/07/2021	SmPC, Labelling and PL	Modifications of the product information: [Section 4.4] Endophthalmitis, intraocular inflammation, traumatic cataract, retinal detachment, retinal vasculitis, and/or retinal vascular occlusion. Addition of: Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of Beovu. In patients developing these events, treatment with Beovu should be discontinued and the events should be promptly

					managed. [Section 4.8] Addition of: Retinal vascular occlusion, frequency not known. Addition of: Retinal vasculitis, frequency not known. For more information, please refer to the Summary of Product Characteristics.
IB/0004	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	11/08/2020	n/a		
IB/0001	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)	11/05/2020	19/07/2021	SmPC	