Ervebo

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
II/0022/G	This was an application for a group of variations. 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	14/07/2022		Annex II	Annex II.A has been updated to remove the text regarding the time-limited exemption allowing reliance on batch control testing conducted in the registered site(s) that are located in a third country. The transfer of the finished product quality control testing release test methods to laboratories located in the EU has been completed.

[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).

	product and any of the test methods at the site is a biol/immunol method B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IG/1515	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	14/06/2022	n/a		
PSUSA/10834 /202111	Periodic Safety Update EU Single assessment - recombinant vesicular stomatitis virus - Zaire ebolavirus vaccine (live)	10/06/2022	n/a		PRAC Recommendation - maintenance
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/04/2022		PL	
IB/0020/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure 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.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	16/03/2022	n/a		

	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
PSUSA/10834 /202105	Periodic Safety Update EU Single assessment - recombinant vesicular stomatitis virus - Zaire ebolavirus vaccine (live)	02/12/2021	n/a		PRAC Recommendation - maintenance
IB/0018	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	28/09/2021	n/a		
IB/0017	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	14/09/2021	n/a		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/07/2021	31/01/2022	PL	
IB/0015	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	02/07/2021	n/a		
PSUSA/10834 /202011	Periodic Safety Update EU Single assessment - recombinant vesicular stomatitis virus - Zaire ebolavirus vaccine (live)	10/06/2021	n/a		PRAC Recommendation - maintenance
IA/0013	B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	26/04/2021	n/a		

IB/0012/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure 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	15/03/2021	n/a		
IA/0011	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	18/02/2021	n/a		
IB/0009	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	26/01/2021	n/a		
II/0008/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 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	12/11/2020	14/01/2021	SmPC, Annex II and PL	As a result of this group of quality variations, all specific obligations laid down in Annex II have been fulfilled and comprehensive data supports a favourable benefit-risk balance of the medicinal product Ervebo. Pursuant to Article 14-a(8) of Regulation (EC) No 726/2004, the CHMP recommends by consensus the granting of a marketing authorisation in accordance with Article 14(1) of Regulation (EC) No 726/2004 for Ervebo. Consequently, section 5.1 of the SmPC has been updated to delete the reference to "Conditional Approval" scheme

					and Annex II E has been updated to delete Specification Obligations to complete post-authorisation measures for the conditional marketing authorisation. The Package Leaflet is updated accordingly. Due to extensive commercial confidential information enclosed in the Assessment Report for quality variations, this is not available to public access.
II/0007/G	This was an application for a group of variations. C.I.4: To update section 5.1 of the SmPC with the description and final results from study V920-018; this is a phase 3 open-label trial conducted in Guinea to evaluate the safety and immunogenicity of Ervebo in vaccinated frontline workers 18 years of age and older that was implemented as Part B of the Phase 3 ring vaccination study V920-010. With this submission, REC 20 is fulfilled. C.I.4: To update section 5.1 of the SmPC based on the result of the final study reports on the Correlate of Protection. With this submission, REC 16 is fulfilled. C.I.4: To update section 5.1 of the SmPC, based on results from the integrated summary of immunogenicity (ISI). With this submission, RECs 15 and 22 are fulfilled. C.I.13: Submission of Non-Human Primates (NHP) Correlate of Protection analysis report (non-clinical report). Analysis is based upon previous submitted	14/01/2021	31/01/2022	SmPC, Labelling and PL	Protocol 018 was a Phase 3 open-label trial conducted in Guinea to evaluate the safety and immunogenicity of Ervebo in vaccinated frontline workers 18 years of age and older that was implemented as Part B of the Phase 3 ring vaccination study for Protocol 010. In this trial, a total of 2,115 subjects were enrolled and 2,016 subjects were vaccinated with Ervebo. An immunogenicity sub-study included 1,217 subjects who were vaccinated and provided samples for the assessment of immunogenicity. Immunogenicity data were obtained in Protocol 009 in Liberia, Protocol 011 in Sierra Leone, Protocol 012 in the United States, Canada, and Europe, and Protocol 018 in Guinea. Gamma irradiation of specimens (from regions involved in Ebola outbreaks) was performed to reduce risk of wild-type Ebola virus infection of laboratory workers, but increased pre-vaccination GP-ELISA immune responses by approximately 20% and decreased post-vaccination GP-ELISA and PRNT immune responses by approximately 20%. Gamma irradiation, baseline seropositivity and other factors result in a higher immune response in Protocol 012. For more information, please refer to the Summary of Product Characteristics.

	NHP studies which are already part of the dossier. The MAH takes the opportunity to implement changes in the Package Leaflet following the assessment of the User Acceptance Test, procedure EMEA/H/C/004554/REC/011. With the implementation of these changes to the PL, the MAH fulfils REC011. In addition, minor editorial changes have been included in the SmPC and patient leaflet. 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 C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10834 /202005	Periodic Safety Update EU Single assessment - recombinant vesicular stomatitis virus - Zaire ebolavirus vaccine (live)	26/11/2020	n/a		PRAC Recommendation - maintenance
R/0004	Renewal of the marketing authorisation.	23/07/2020	15/09/2020	Annex II	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this

					medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Ervebo, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. The CHMP considered that process validation data were provided demonstrating that the active substance process is properly validated. Comparability data confirmed that the commercial product manufactured at the Burgwedel site is representative of the material used in the clinical trials. Additional qualification data were provided for a critical reagent used in the identity test ensuring proper quality control of the active substance and the finished product. An in-process control for total protein with appropriate acceptance was introduced for the active substance, ensuring proper quality control of the active substance. Based on the data submitted, the CHMP concluded that the respective specific obligations have been resolved and can be deleted from the Annex II.
IB/0006	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation	03/08/2020	n/a		
IB/0003	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	05/06/2020	n/a		
IB/0002/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of	04/06/2020	n/a		

	the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IB/0001	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	20/02/2020	n/a		