Rybrevant

Procedural steps taken and scientific information after the authorisation*

*Due to the Agency`s update of its procedure management systems, an additional document, reflecting the historical lifecycle may be available in the 'Assessment history' section. For the complete product lifecycle procedures, you may need to also refer to **EPAR - Procedural steps taken and scientific information after authorisation (archive)**.

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
Variation type IB /	Outcome:	26/05/2026			

[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).

EMA/VR/0000341966	This was an application for a group of variations. Q.I.a.2 Change in the manufacturing process of the active substance, intermediate of an active substance or starting materials for biological active substance - Q.I.a.2.a) Minor change in the manufacturing process - Accepted Q.I.a.2 Change in the manufacturing process of the active substance, intermediate of an active substance or starting materials for biological active substance - Q.I.a.2.a) Minor change in the manufacturing process - Accepted Q.I.d.1.a) Re-test period/storage period - Q.I.d.1.a.5 Extension of a re-test period/storage period supported by real time data fully in line with the stability protocol - Accepted				
Variation type IA / EMA/VR/0000331964	Outcome: Q.I.b.2 Change to analytical procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - Q.I.b.2.a) Minor change to an analytical procedure for the active substance - Accepted	06/03/2026			

Extension of marketing authorisation / EMA/X/0000268898	Outcome: This was an application for a group of variations. 2. Changes to strength, pharmaceutical form and route of administration - (c) change or addition of a new strength/potency - Accepted B.II.c.4 Change in synthesis or recovery of a nonpharmacopoeial excipient (when described in the dossier) or a novel excipient - B.II.c.4.c The excipient is a biological/immunological substance - Accepted B.II.e.7 Change in supplier of packaging components or devices (when mentioned in the dossier) - B.II.e.7.b Replacement or addition of a supplier - Accepted B.I.b.2 Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - B.I.b.2.e Other changes to a test procedure (including replacement or addition) for the active substance or a starting material/intermediate - Accepted B.I.a.3 Change in batch size (including batch size ranges) of active substance or intermediate used in the manufacturing process of the active substance - B.I.a.3.c The change requires assessment of the comparability of a biological/immunological	11/12/2025	20/02/2026	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion EMA/X/0000268898

	active substance - Accepted B.I.a.1 Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier - B.I.a.1.e The change relates to a biological active substance or a starting material/reagent/intermediate used in the manufacture of a biological/immunological product - Accepted C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted				
Variation type IB / EMA/VR/0000287530	Outcome: This was an application for a group of variations. B.I.a.2 Changes in the manufacturing	13/10/2025			

	process of the active substance - B.I.a.2.a Minor change in the manufacturing process of the active substance - Accepted B.I.b.2 Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - B.I.b.2.a Minor changes to an approved test procedure - Accepted B.I.a.2 Changes in the manufacturing process of the active substance - B.I.a.2.z Other variation - Accepted				
Variation type II / EMA/VR/0000287115	Outcome: This was an application for a group of variations. B.II.d.2 Change in test procedure for the finished product - B.II.d.2.d Other changes to a test procedure (including replacement or addition) - Accepted B.II.d.1 Change in the specification parameters and/or limits of the finished product - B.II.d.1.f Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product - Accepted	02/10/2025			
Variation type II / EMA/VR/0000261993	Outcome: This was an application for a variation	18/09/2025	20/02/2026	SmPC and PL	SmPC new text Based on the results of a phase 2 study in patients treated with amivantamab in

	following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 4.2, 4.4 and 4.8 of the SmPC for Rybrevant and Lazcluze in order to include updated information on enhanced dermatologic management regimen as prophylactic treatment to reduce the risk of dermatological toxicities during treatment, based on results from study 61186372NSC2007. Study 61186372NSC2007 (COCOON) is a Phase 2, open-label, randomized trial evaluating the impact of enhanced versus standard dermatologic management on selected dermatologic adverse events among patients with locally advanced or metastatic EGFR-mutated NSCLC treated first-line with amivantamab + lazertinib. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor corrections to the PI for Lazcluze and Rybrevant.				combination with lazertinib assessing the use of prophylactic therapy with an oral antibiotic, a topical antibiotic on the scalp, a moisturiser on the face and whole body and an antiseptic on hands and feet, recommendations on dermatologic management have been strenghten in sections 4.2 and 4.4 of the SmPC of both products. Prophylactic therapy with oral and topical antibiotics is recommended to reduce the risk and severity of skin and nail reactions in patients receiving amivantamab and lazertinib at treatment initiation. Non comedogenic skin moisturiser (ceramide based or other formulations that provide long lasting skin hydration and exclude drying agents are preferred) on the face and whole body (except scalp) and chlorhexidine solution to wash hands and feet are also recommended beginning on day1 and continued foe the duration of treatment. For more information, please refer to the Summary of Product Characteristics.

Variation type IB / EMA/VR/0000278107	Outcome: This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1 Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier - B.I.a.1.f Changes to quality control testing arrangements for the active substance-replacement or addition of a site where batch control/testing takes place - Accepted	04/09/2025			
PSUR / EMA/PSUR/0000248975	EURD: PSUSA/00010977/202411 Active substance: amivantamab Outcome: Variation In view of available data on skin ulcer from clinical trials, the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between amivantamab and skin ulcer is at least a reasonable possibility. The PRAC concluded that the product information of products containing amivantamab should	19/06/2025	21/08/2025	SmPC and PL	Variation

	be amended accordingly.				
Variation type II / EMA/VR/0000253354	Outcome: This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of section 5.1 of the SmPC in order to provide final Overall Survival (OS) data following Rybrevant extension of indication procedure (EMEA/H/C/005454/II/0013), and Lazcluze MAA approval (EMEA/H/C/006074/0000), and based on final results from study 73841937NSC3003 (MARIPOSA); this is a pivotal randomized, open-label, Phase 3 study that compares the efficacy and safety of the combination of amivantamab and lazertinib (Arm A) versus osimertinib monotherapy (Arm B) and lazertinib monotherapy (Arm C) in participants with EGFRm NSCLC.	19/06/2025	21/08/2025	SmPC	SmPC new text OS, intracranial ORR and DOR data were updated in section 5.1 of the SmPC based on final results from the Mariposa study (a pivotal randomized, open-label, Phase 3 study that compares the efficacy and safety of the combination of amivantamab and lazertinib (Arm A) versus osimertinib monotherapy (Arm B) and lazertinib monotherapy (Arm C) in participants with EGFRm NSCLC): The final analysis of OS demonstrated a statistically significant improvement in OS for Rybrevant in combination with lazertinib compared to Osimertinib and the intracranial ORR and DOR were updated. For more information, please refer to the Summary of Product Characteristics.
Variation type IB / EMA/VR/0000272581	Outcome: B.II.f.1.b Extension of the shelf life of the	18/06/2025	21/08/2025	SmPC	

	finished product - B.II.f.1.b.5 Extension of the shelf-life of a biological/ immunological medicinal product in accordance with an approved stability protocol - Accepted				
Variation type II / EMA/VR/0000257307	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 4.2 and 4.8 of the SmPC in order to change posology recommendations for the premedication regimen to include a higher and extended dose regimen of oral dexamethasone, in addition to the currently approved labelled 20 mg to reduce the incidence and severity of amivantamab-related infusion related reactions (IRRs), based on results from the SKIPPirr study (61186372NSC2005). This is a Phase 2, proof-of-concept, open label, multicentre study conducted in participants with EGFR exon 19deletion or L858R mutated NSCLC who have progressed on or after prior osimertinib and on or after platinum chemotherapy. This study aimed to assess the use of 4 independent pretreatment medication regimens for the	22/05/2025	30/07/2025	SmPC and PL	SmPC new text Based on the results of a phase 2 open-label multicenter study in patients with NSCLC, premedication strategy for Rybrevant has been revised in section 4.2 of the SmPC as follows: During the two days prior to the initial Rybrevant infusion, patients should receive 8 mg dexamethasone orally, twice daily. On the day of the initial infusion (Week 1, Day 1), patients should receive 8 mg dexamethasone orally, one hour prior to infusion in addition to intravenous dexamethasone to further reduce the risk of IRRs. Section 4.8 of the SmPC has also been revised in order to state that with the addition of oral dexamethasone, a 22.5% incidence of IRRs and no grade ≥3 IRRs were reported on the day of the initial infusion. For more information, please refer to the Summary of Product Characteristics.

	prophylaxis of amivantamab-related IRRs. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.				
Variation type IB / EMA/VR/0000265968	Outcome: B.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance - B.I.a.4.b Addition of a new in-process test and limits - Accepted	15/05/2025			
PSUR / EMA/PSUR/0000296559	EURD: PSUSA/00010977/202505 Active substance: amivantamab Outcome: Maintenance	15/01/2026			Maintenance