Rybrevant

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
X/0014	Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(e) Change or addition of a new route of administration	30/01/2025	04/04/2025	SmPC, Labelling and PL	Please refer to Scientific Discussion Rybrevant EMEA/H/C/005454/X/014.

[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).

II/0018/G	This was an application for a group of variations. 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.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.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.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other	13/03/2025	n/a		

	variation B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products 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.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size				
PSUSA/10977 /202405	Periodic Safety Update EU Single assessment - amivantamab	16/01/2025	n/a		PRAC Recommendation - maintenance
II/0013	Extension of indication to include amivantamab in combination with lazertinib for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with EGFR exon 19 deletions or exon 21 L858R substitution mutations (EGFRm NSCLC), based on results from study 73841937NSC3003 (MARIPOSA). This is a 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 primary objective of the MARIPOSA study was to assess the efficacy of the combination	14/11/2024	19/12/2024	SmPC and PL	Please refer to Scientific Discussion 'Rybrevant-H-C-005454-II-0013'.

	of amivantamab and lazertinib (Arm A), compared with osimertinib (Arm B), as measured by PFS assessed by BICR in adult participants with EGFRm NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.2 of the EU RMP has also been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0017/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 of the AS	30/09/2024	n/a		
II/0011	Extension of indication to include amivantamab in combination with carboplatin and pemetrexed for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) Exon 19 deletions or Exon 21 L858R substitution mutations after failure of prior therapy including an EGFR tyrosine kinase inhibitor (TKI) for RYBREVANT, based on the final results from study 61186372NSC3002 (MARIPOSA 2); this is a randomized, open label, multicenter Phase 3 study	25/07/2024	22/08/2024	SmPC and PL	Please refer to Scientific Discussion Rybrevant-H-C-5454-II-11.

	that compares efficacy and safety of amivantamab in combination with carboplatin and pemetrexed (ACP) with carboplatin and pemetrexed (CP). The primary objective of the MARIPOSA 2 study is to compare efficacy, as demonstrated by PFS, in participants treated with ACP versus CP alone. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2 of the EU RMP has also been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0010	Extension of indication to include amivantamab in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal-growth factor receptor (EGFR) Exon 20 insertion mutations for RYBREVANT, based on the final results from study 61186372NSC3001 listed as a Specific Obligation in the Annex II of the Product Information; this is a global, open-label, randomized Phase 3 study of ACP compared to CP alone in participants with newly diagnosed, locally advanced or metastatic NSCLC characterized by EGFR exon 20ins. The primary objective of the PAPILLON study is to compare efficacy, as demonstrated by PFS, in participants treated with ACP versus CP alone. As a consequence, sections 4.1, 4.2, 4.8, 4.9, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package	25/04/2024	27/06/2024	SmPC, Annex II and PL	Please refer to Scientific Discussion: Rybrevant-H-C-5454-II-0010.

	Leaflet is updated in accordance. Version 3.1 of the RMP has also been agreed. In addition, the MAH took the opportunity to update Annex II and Annex IV of the PI. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation given the fulfilment of the SOB. As part of the application, the MAH also requested an extension of the market protection by one additional year. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10977 /202311	Periodic Safety Update EU Single assessment - amivantamab	13/06/2024	n/a		PRAC Recommendation - maintenance
PSUSA/10977 /202305	Periodic Safety Update EU Single assessment - amivantamab	11/01/2024	n/a		PRAC Recommendation - maintenance
IB/0009/G	This was an application for a group of variations. 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 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	20/09/2023	16/05/2024	SmPC and PL	

R/0007	Renewal of the marketing authorisation.	20/07/2023	11/09/2023		
PSUSA/10977 /202211	Periodic Safety Update EU Single assessment - amivantamab	08/06/2023	n/a		PRAC Recommendation - maintenance
PSUSA/10977 /202205	Periodic Safety Update EU Single assessment - amivantamab	12/01/2023	n/a		PRAC Recommendation - maintenance
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	30/11/2022	n/a		
IB/0005	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	29/11/2022	11/09/2023	SmPC and Annex II	
R/0002	Renewal of the marketing authorisation.	21/07/2022	26/09/2022		
II/0001	Update of section 4.8 of the SmPC in order to add hypokalaemia and hypomagnesaemia to the list of adverse drug reactions (ADRs), with the frequency common, based on an updated analysis of data submitted during the marketing authorisation procedure. The Package Leaflet is updated accordingly. In addition, the MAH proposed to update the current information in section 4.2 of the SmPC to improve clarity and provide more specific guidance. Section 4.4 was updated to also reflect ILD-like adverse reactions. The MAH also took the opportunity to introduce editorial changes in section 4.8 of the SmPC.	07/07/2022	26/09/2022	SmPC and PL	Section 4.8 of the SmPC has been updated to add hypokalaemia and hypomagnesaemia to the list of adverse drug reactions (ADRs), with the frequency common, based on a reanalysis of data submitted during the initial marketing authorisation procedure. Section 4.2 of the SmPC has been updated to clarify recommendations for dose reductions. Sections 4.2 and 4.4 of the SmPC were harmonized to reflect consistently ILD and ILD-like reactions. In addition, examples of Grade 4 skin reactions were removed from section 4.2 of the SmPC. Finally, in Section 4.8 of the SmPC, the word “paronychia” has been replaced by “nail toxicity”. For more information, please

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				refer to the Summary of Product Characteristics.