HETRONIFLY

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 II /	Outcome:	21/05/2026	19/06/2026	SmPC and PL	Please refer to Scientific Discussion

[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/0000290021	C.I.6 Change(s) to therapeutic indication(s) - C.I.6.a Addition of a new therapeutic indication or modification of an approved one - Accepted Extension of indication to include HETRONIFLY in combination with carboplatin and nab-paclitaxel for the first-line treatment of adult patients with unresectable, locally advanced or metastatic squamous non-small cell lung carcinoma based on final results from study HLX10-004-NSCLC303; this is a randomized, double-blind, multi-center, phase III pivotal study, to compare the clinical efficacy and safety of serplulimab combined with chemotherapy (carboplatin and nab-paclitaxel) versus placebo combined with chemotherapy (carboplatin and nab-paclitaxel). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP Version 3.0 is agreed.				EMA/VR/0000290021
Variation type II / EMA/VR/0000282407	Outcome: C.I.6 Change(s) to therapeutic indication(s) - C.I.6.a Addition of a new therapeutic indication or modification of an approved one - Accepted Extension of indication to include HETRONIFLY in combination with carboplatin	26/03/2026	30/04/2026	SmPC and PL	Please refer to Scientific Discussion EMA/VR/0000282407

	and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung carcinoma who do not have EGFR or ALK positive mutations based on results from study HLX10-002-NSCLC301. As a consequence, sections 4.1, 4.2, 4,4, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been approved.				
Variation type II / EMA/VR/0000284402	Outcome: C.I.6 Change(s) to therapeutic indication(s) - C.I.6.a Addition of a new therapeutic indication or modification of an approved one - Accepted Extension of indication to include, in combination with fluoropyrimidine- and platinum-based chemotherapy, the first-line treatment of adult patients with unresectable, locally advanced, recurrent or metastatic oesophageal squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 5 for HETRONIFLY, based on results from study HLX10-007-EC301; this is a randomized, double-blind, multi-center, phase III clinical study comparing the clinical efficacy and safety of HLX10 or placebo combined with chemotherapy in first-line treatment of locally advanced/metastatic	26/03/2026	30/04/2026	SmPC and PL	Please refer to Scientific Discussion EMA/VR/0000284402

	esophageal squamous cell carcinoma (ESCC) patients. 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 2.0 of the RMP has also been submitted.				
Variation type IA_IN / EMA/VR/0000326671	Outcome: Q.II.b.1 Change in the manufacturing site for part or all of the manufacturing process of the finished product (except for batch release and batch control testing sites) - Q.II.b.1.a) Addition or replacement of a site responsible for secondary packaging - Accepted	11/02/2026			
Variation type IA / EMA/VR/0000321496	Outcome: This was an application for a group of variations. B.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance - B.I.a.4.a Tightening of in-process limits - 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.b.2 Change in test procedure for active substance or starting	12/01/2026			

	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.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product - B.II.b.3.a Minor change in the manufacturing process - Accepted B.II.e.6 Change in any part of the (primary) packaging material not in contact with the finished product formulation (such as colour of flip-off caps, colour code rings on ampoules, change of needle shield (different plastic used)) - B.II.e.6.b Change that does not affect the product information - Accepted				
Variation type II / EMA/VR/0000291455	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, 4.4 and 4.8 of SmPC in order to include myasthenia gravis and myasthenic syndrome to the list of adverse drug reactions (ADRs) with frequency "rare", based on a signal assessment report. Additional warning and recommendations for treatment modifications are also included.	04/12/2025	30/04/2026	SmPC and PL	SmPC new text Based on safety signals identified during routine pharmacovigilance activities, "myasthenia gravis" and "myasthenic syndrome" have been included as ADRs. Section 4.4 has been updated to include a warning advising patients to seek immediate medical attention if symptoms of myasthenia gravis and myasthenic syndrome occurs (e.g. muscle weakness and tiring easily). Section 4.2 has been updated to include recommendations for treatment modifications: in Grade 3 or 4 cases, treatment should be permanently discontinued, while in Grade 2 cases, treatment should be withheld.

	The Package Leaflet is updated accordingly. The updated RMP version 1.4 has also been submitted.				
Variation type IB / EMA/VR/0000301620	Outcome: This was an application for a group of variations. B.II.b.4 Change in the batch size (including batch size ranges) of the finished product - B.II.b.4.f The scale for a biological/immunological medicinal product is increased / decreased without process change (e.g. duplication of line) - Accepted B.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product - B.II.b.3.a Minor change in the manufacturing process - Accepted	03/11/2025			
Variation type IB / EMA/VR/0000272312	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.z Other variation - Accepted C.I.z - To update section 2 of the SmPC and section 2 of the package leaflet to include polysorbate 80 as an excipient as per the Excipients Guideline. - To update sections 4.2, 4.4, 4.5, 4.8, 5.2, 5.3 and 6.1 of the SmPC, annex IID, and section 4 of the package leaflet in order to implement	25/07/2025	30/04/2026	SmPC, Annex II and PL	

	changes proposed by member states Spain and Germany as part of the post-opinion linguistic review of the MAA application. - In addition, the MAH has taken the opportunity to update Part B of Annex II to revise the legal status of Hetronifly from "special and restricted medical prescription" to "restricted medical prescription" in order to align the PI with the RMP.				
Variation type IB / EMA/VR/0000281029	Outcome: This was an application for a group of variations. 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.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.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	11/07/2025			

	no Ph. Eur. Certificate of Suitability is part of the approved dossier - B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation - Accepted				
Variation type IA_IN / EMA/VR/0000266638	Outcome: This was an application for a group of variations. B.II.b.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - B.II.b.1.a Secondary packaging site - Accepted B.II.b.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - B.II.b.1.a Secondary packaging site - Accepted B.II.b.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - B.II.b.1.a Secondary packaging site - Accepted B.II.b.1 Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - B.II.b.1.a Secondary packaging site - Accepted B.II.b.2.c Replacement or addition of a	05/05/2025	30/04/2026	Annex II and PL	

	manufacturer responsible for importation and/or batch release - B.II.b.2.c.1 Not including batch control/testing - Accepted B.II.b.2.c Replacement or addition of a manufacturer responsible for importation and/or batch release - B.II.b.2.c.1 Not including batch control/testing - Accepted				
Marketing Authorisation Transfer - H / EMA/T/0000252778	Outcome: transfer of marketing authorisation from Henlius Europe GmbH to Accord Healthcare S.L.U.	26/02/2025	31/03/2025	SmPC, Labelling and PL	
PSUR / EMA/PSUR/0000317684	EURD: PSUSA/00011112/202509 Active substance: serplulimab Outcome: Maintenance	10/04/2026			Maintenance
PSUR / EMA/PSUR/0000282289	EURD: PSUSA/00011112/202503 Active substance: serplulimab Outcome: Maintenance	30/10/2025			Maintenance