Enhertu

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 / EMA/VR/0000340512	Outcome: C. Safety, efficacy, pharmacovigilance changes - C.4 Change(s) in the summary of product characteristics, labelling or	25/06/2026		SmPC	Section 5.2 'Pharmacokinetic properties' of the SmPC Biotransformation

[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).

	package leaflet due to new quality, preclinical, clinical or pharmacovigilance data. - Accepted Update of section 5.2 of the SmPC in order to update biotransformation information based on results from non-clinical studies AE-8104-G (Identification of cytochrome P450 isoforms involved in metabolism of MAAA-1181d) and AE-8795-G (uridine diphosphate-glucuronosyltransferases (UGT) Metabolic stability of MAAA-1181d in Human, Monkey and Rat Liver Microsomes).				Trastuzumab deruxtecan undergoes intracellular cleavage by lysosomal enzymes to release the DXd. The humanised HER2 IgG1 monoclonal antibody is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG. In vitro metabolism studies in human liver microsomes indicate that DXd is metabolised mainly by CYP3A4 via oxidative pathways and does not undergo significant metabolism by uridine diphosphate-glucuronosyltransferases (UGT) or other CYP enzymes. For more information, please refer to the Summary of Product Characteristics.
Variation type IA / EMA/VR/0000350663	Outcome: 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 - Refused	22/06/2026			
Variation type IB / EMA/VR/0000343022	Outcome: This was an application for a variation following a worksharing procedure according to Article 20 of Commission	18/06/2026			

	Regulation (EC) No 1234/2008. Q.I.a.1 Change in the manufacturing site of a starting material/intermediate used in the manufacturing process of the active substance or change in the manufacturing site (including where relevant quality control testing sites) of the active substance - Q.I.a.1.i) Addition or replacement of a batch control/testing site of the active substance or starting material/intermediate used in the manufacturing of a biological active substance, applying a biological/immunological/immunochemical analytical procedure - Accepted				
Variation type II / EMA/VR/0000293327	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 treatment of adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumours who have received prior treatment and who have no satisfactory alternative treatment options for Enhertu, based on results from study D967VC00001 (DESTINY-PanTumor02);	21/05/2026	25/06/2026	SmPC and PL	Please refer to Scientific Discussion EMA/VR/0000293327.

	this is a Phase II, multicenter, open-label study to evaluate the efficacy and safety of trastuzumab deruxtecan for the treatment of selected HER2-expressing tumours; 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 11 of the RMP has also been agreed. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial changes to the PI.				
Variation type II / EMA/VR/0000328212	Outcome: Q.II.f.1 Change in the shelf life or storage - Q.II.f.1.c Change in storage conditions of a biological finished product - Accepted	30/04/2026	25/06/2026	SmPC, Labelling and PL	The SmPC section 6.4 has been updated as follows: Store in a refrigerator (2 ºC - 8 ºC). Do not freeze. Store in the original carton in order to protect from light Section 5 of the Package Leaflet and Annex III.A outer carton are updated accordingly. The Applicant took the opportunity to include the date of the latest renewal in section 9 of the SmPC.
Variation type IB / EMA/VR/0000323851	Outcome: This was an application for a group of variations. B.I.a.2 Changes in the manufacturing process of the active substance - B.I.a.2.a Minor change in the manufacturing process of the active substance - Accepted B.I.a.4 Change to in-process tests or limits	12/03/2026			

	applied during the manufacture of the active substance - B.I.a.4.z Other variation - Accepted B.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance - B.I.a.4.z Other variation - Accepted B.I.a.4 Change to in-process tests or limits applied during the manufacture of the active substance - B.I.a.4.z Other variation - Accepted B.I ACTIVE SUBSTANCE - B.I.z Other variation - Accepted				
Variation type IA_IN / EMA/VR/0000319753	Outcome: 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.a The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer - Accepted A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF	23/01/2026			

	holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted				
Variation type IA / EMA/VR/0000314238	Outcome: A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in	03/12/2025			

	the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted				
Variation type IA / EMA/VR/0000310421	Outcome: A.5 Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites) - A.5.b The activities for which the manufacturer/importer is responsible do not include batch release - Accepted	27/11/2025			
Variation type II / EMA/VR/0000281778	Outcome: 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	13/11/2025			

Renewal - 1 year / EMA/R/0000282648	Outcome:	18/09/2025	21/11/2025	SmPC, Annex II and PL	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 Enhertu, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Sections 4.8, 5.1 and 5.2 of the SmPC as well as section 4 of the Package Leaflet have been updated to reflect the final results from study DS-8201-A-U306 (DESTINY-Gastric04) in order to fulfil SOB 006.1. This is a phase 3, multicentre, 2-arm, randomised, open-label study of Enhertu in subjects with HER2-positive metastatic and/or unresectable gastric or gastroesophageal junction (GEJ) adenocarcinoma that has progressed on or after a trastuzumab-containing regimen. Annex II.E was also amended to delete SOB 006.1 which is considered fulfilled as part of this annual renewal as well as to update the due date for specific obligation SOB 007 pertaining to study D967SC00001 (DESTINY-Lung04 study) from Q4 2025 to Q4 2026 due to slower than expected

					accrual of PFS by BICR events. Version 10.0 of the RMP has also been submitted. In addition the MAH took the opportunity to include the missing reference to E433 for polysorbate 80 in section 6 of the Package Leaflet, to update the contact details of the Icelandic local representative in the Package Leaflet and to correct some translations mistakes in the BG, CZ, DA, DE, EL, ES, ET, FI, FR, HR, IS, IT, LT, LV, MT, NL, NO, PL, PT, SK, SL and SV annexes.
Variation type IB / EMA/VR/0000291445	Outcome: This was an application for a group of variations. B.I ACTIVE SUBSTANCE - B.I.z Other variation - Accepted B.II. FINISHED PRODUCT - B.II.z Other variation - Accepted	27/08/2025			
Variation type IA / EMA/VR/0000279297	Outcome: A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of	26/06/2025			

	the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted				
Variation type II / EMA/VR/0000263542	Outcome: 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	12/06/2025			
Variation type II / EMA/VR/0000247231	Outcome: B.II.g) Design Space and post approval change management protocol - B.II.g.2 Introduction of a post approval change management protocol related to the finished product - Accepted	05/06/2025			

PSUR / EMA/PSUR/0000257882	EURD: PSUSA/00010894/202412 Active substance: trastuzumab deruxtecan Outcome: Maintenance	10/07/2025			Maintenance
PSUR / EMA/PSUR/0000296589	EURD: PSUSA/00010894/202506 Active substance: trastuzumab deruxtecan Outcome: Maintenance	15/01/2026			Maintenance.
PSUR / EMA/PSUR/0000336128	EURD: PSUSA/00010894/202512 Active substance: trastuzumab deruxtecan Outcome: Maintenance	09/07/2026			