EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Enhertu

Date: July 2024

Assessment report

Enhertu

Unit: Technical Assessment Unit

Administrative information:

Trade name of the medicinal product:	Enhertu
INN (or common name) of the active substance(s):	Trastuzumab Deruxtecan 100 mg
Manufacturer of the finished product	Baxter Oncology GmbH, Kantstrasse 2, 33790 Halle / Westfalen, Germany
Marketing Authorization holder	Daiichi Sankyo Europe GmbH , Zielstattstrasse 48, 81379 Munich - GERMANY
Applied Indication(s):	Enhertu is indicated for: **HER2-positive breast cancer** Enhertu as monotherapy is indicated for the treatment of adult patients with unrespectable or metastatic HER2-positive breast cancer whohave received one or more prior anti-HER2- based regimens. **HER2-low breast cancer** Enhertu as monotherapy is indicated for the treatment of adult patients with unrespectableor metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. **Non-small cell lung cancer (NSCLC)** Enhertu as monotherapy is indicated for the treatment of adult patients with advanced NSCLC whose tumours have an activating HER2 (ERBB2) mutation and who require systemic therapy following platinum-based chemotherapy with or without immunotherapy. **Gastric cancer** Enhertu as monotherapy is indicated for the treatment of adult patients with

	advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab- based regimen.
Pharmaceutical form(s) and strength(s):	-powder for concentrate for solution forinfusion -Strength: 100 mg powder of trastuzumab deruxtecan.
Route of administration	Intravenous infusion
Approved pack	Carton box containing one amber borosilicate glass (type I) vial, and sealed with a fluoro-resin laminated butyl rubber stopper, and a polypropylene/ aluminum yellow flip-off crimp cap & an insert leaflet

List of abbreviations

ADC	antibody-drug conjugate
CHO	Chinese Hamster Ovary
DP	Drug Product
DS	Drug substance
GMP	Good manufacturing practice
HER2	Human epidermal growth factor receptor 2
HR+	Hormone receptor positive
NSCLC	Non-small cell lung cancer
GEJ	gastroesophageal junction

Dossier initial submission and evaluation process.

- -The product was submitted for registration via reliance model level 1
- -The dossier was initially received by the registration administration units on 29.3.2023 after providing EMA detailed assessment report along with Full CTD for the product.

1. **'General introduction about the product including brief description of the AI, its mode of action and indications:**

-Enhertu is an antibody-drug conjugate (ADC) presented as a powder for concentrate for solution forinfusion in a vial containing 100 mg of trastuzumab deruxtecan as active substance in a 10 mL Type 1 amber borosilicate glass vial sealed with a fluoro-resin laminated butyl rubber stopper, and a polypropylene/aluminium yellow flip off crimp cap.

-Trastuzumab deruxtecan is formulated with L-histidine, L-histidine hydrochloride

monohydrate, sucrose and polysorbate 80. Prior to use, the powder is reconstituted with water for injections. Thereconstituted solution is sterile and intended for single use only.

-DS is an antibody-drug conjugate (ADC) that contains trastuzumab, a humanised anti HER2 IgG1 monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells, covalently linked to a topoisomerase I inhibitor via a linker. Approximately 8 molecules of deruxtecan are attached to eachantibody molecule.

-the DP is used as monotherapy for the treatment of adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvantchemotherapy. Patients with hormone receptor positive (HR+) breast cancer must additionally have received or must be ineligible for endocrine therapy.

2. **Quality aspects:**

- **Manufacturer(s):**
  -Enhertu Drug substance is manufactured at Daiichi Sankyo Chemical Pharma Co.,ltd and Lonza AG Lonzastrasse ,2 Visp 3930-Switzerland
  -Enhertu as finished product is manufactured at Baxter Oncology GmbH, – GERMANY
  - Manufacturing of both DS and DP are performed in accordance with cGMP regulations.
- **Stability**
  Drug substance :
  - **Approved shelf life**: 36 Month
  -**Approve storage conditions**: Store in original container in order to protect from light at -20 ◦ C to ±5 ◦ C.
  Drug Product:
  -**Approved shelf life**: 4 years

- **Approve storage conditions**: Store at temperature between 2-8 0C, Don't Freeze. Swirl the vial gently until completely dissolved. Do not shake.

3. Non-clinical and clinical aspects:

-Overall, the primary pharmacodynamic studies provided adequate evidence that trastuzumab deruxtecan show anti-tumor activity against both HER2 positive and HER2 low cancer models. The pharmacokinetic programme was considered sufficient. Toxicology studies showed that trastuzumab deruxtecan was tolerated in both rats and cynomolgus at clinically relevant as well as higher exposures.

- In conclusion the overall benefit/risk of Enhertu (Powder for concentrate for solution for infusion, 100 mg, Intravenous infusion) is favorable as monotherapy for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received one or more prior anti HER2 based regimens, metastatic HER2-low breast cancer, Non-small cell lung cancer and advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab- based regimen.

- **General Conclusion and Recommendations if any:**

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/enhertu-epar-public-assessment-report_en.pdf