EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Herzuma 150mg

Date: March 2024

Unit: Technical Assessment Unit

Assessment report

Herzuma

Administrative information:

Trade name of the medicinal product:	Herzuma
INN (or common name) of the active substance:	Trastuzumab 150mg
Manufacturer of the finished product	Celltrion, Inc., plant II (CLT2) 20, Academy-ro 51 beon-gil, Yeonsu-gu Incheon, Republic of Korea.
Marketing Authorization holder	Celltrion, Inc., 20 Academy-ro 51 beon-gil, Yeonsu-gu Incheon, Republic of Korea.
Applied Indication(s):	-Metastatic Breast Cancer (MBC) -The treatment of adult patients with HER2-positive early breast cancer (EBC) -In combination with capecitabine or 5-fluorouracil and cisplatin is indicated for the treatment of adult patients with HER2-positive metastatic adenocarcinoma of the stomach or gastroesophageal junction who have not received prior anti-cancer treatment for their metastatic disease.
Pharmaceutical form(s) and strength(s):	- The product is formulated as a sterile, white to pale yellow lyophilised powder containing 150 mg of CT-P6 drug substance. -the lyophilized powder is reconstituted with 7.2 mL of sterile water for injection (SWFI) to yield a single dose formulation containing 21 mg/mL trastuzumab, at pH 6.0.
Route of administration	intravenous (IV) administration
Approved Pack	Carton box containing a 20 ml type one borosilicate glass vial without plasma coating, closed with chlorobutyl rubber stopper I and 20 mm aluminium seal with a flip-off button.

	And Carton box containing a 20 ml type one borosilicate glass vial with plasma coating, closed with chlorobutyl rubber stopper II and 20 mm aluminium seal with a flip-off button

List of abbreviations:

cGMP	Current Good Manufacturing Practice
CLT2	Celltrion, Inc., plant II
CT-P6	Trastuzumab (Celltrion)
EBC	early breast cancer
EMA	European medicines agency
HER2	Human epidermal growth factor-2
I.V	Intravenous
MBC	Metastatic Breast Cancer
sWFI	sterile water for injection
PD	pharmacodynamic
PK	pharmacokinetic

Dossier initial submission and evaluation process:

- The product was submitted for registration via Fast Track (343/2021) pathway.
- The dossier evaluation by the registration administration units was started on 21.7.2022 after providing all the required documents according to the "Checklist for documents of new biological products registration file".

1. General introduction about the product

- CT-P6 is a humanised monoclonal IgG1 subclass antibody that selectively binds with high affinity to the extracellular domain of the human epidermal growth factor receptor 2 (HER2).
- The biological activity of Herceptin® is considered to be representative of the mechanism of action and pharmacological effects of CT-P6.
- CT-P6 selectively binds with high affinity to the extracellular domain of the Human Epidermal Growth Factor Receptor 2 (HER2). Binding of CT-P6 to HER2 blocks its dimerisation with the other receptors of the erbB family, and so prevents the consequent receptor activation which leads to tumor cell growth. Moreover, binding of CT-P6 to HER2 prevents the proteolytic cleavage of its extracellular domain and

subsequent activation of its intracellular kinase domain, again preventing HER2 from stimulating a signaling cascade that causes tumor cells to grow.

- The finished product is presented as a sterile, white to pale yellow lyophilised powder containing 150 mg of CT-P6 active substance as the active ingredient.
- The finished product stored in a glass vial with rubber stopper and a flip-off seal.
- Herzuma has been developed as a similar biological medicinal product to the innovator product Herceptin® (trastuzumab,….maufacturer) which was approved in the Egyptian market in December 2011.
- Herzuma and Herceptin® are identical with respect to pharmaceutical form, concentration and composition, and route of administration. The only difference is in the concentration of the excipient, trehalose.

2. **Quality aspects:**

- **Manufacturer(s):**

-Both active substance & finished product are manufactured at Celltrion, Inc., plant II (CLT2) 20, Academy-ro 51 beon-gil, Yeonsu-gu Incheon, Republic of Korea in accordance with cGMP.

- **Stability**

Drug substance:

Approved Storage Conditions of the active substance: -40±5°C
Approved shelf life for the active substance: 60 months

Drug product:

Approved Storage Conditions of the finished product:
-Store in a refrigerator (2ºC - 8ºC).
-Do not freeze the reconstituted solution
Approved shelf life for the finished product: 60 months

3. **Non –Clinical aspect & Clinical aspect:**

- The applicant used a stepwise approach in order to demonstrate that CT-P6 is comparable to Herceptin with respect to PD/PK and toxicity.
- Toxicity studies showed no toxicological findings and no difference in response compared to treatment with Herceptin.
- Overall, the non-clinical studies were considered comprehensive and support the comparability exercise to confirm the biosimilarity between CT-P6 and the reference product Herceptin.

- Pharmacology studies have shown similarly where the presented single and multiple dose PK results of CT-P6 versus Herceptin are comparable
- The safety database was mature with most safety data derived from study CT-P6 3.2 and a median follow up of 19.3 months in the CT-P6 treatment group and 19.6 months in the Herceptin treatment group. No new signals were identified and the safety data was supportive of biosimilarity.
- The totality of the data on the comparability exercise indicates that CT-P6 can be considered a biosimilar of Herceptin.
- In conclusion the overall benefit/risk of Herzuma 150 mg (vial) is favorable in the treatment of Metastatic breast cancer, Early breast cancer and Metastatic gastric cancer.

➢ **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/herzuma-epar-public-assessment-report_en.pdf