EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Abevmy 100 mg/4ml
Abevmy 400 mg/16ml

Date: July 2024

Assessment report

Unit: Technical Assessment Unit

Abevmy

Administrative information:

Trade name of the medicinal product:	Abevmy 100 mg/4ml. Abevmy 400 mg/16ml.
INN (or common name) of the active substance(s):	Bevacizumab 25 mg/ml
Manufacturer of the finished product	Biocon Biologics India limited, special economic zone, plot no 2,3,4 and 5 phase IV, Bommasandra-Jigani link road, Bommasandra post, Bengaluru, Karnataka 560099 - INDIA
Marketing Authorization holder	Biosimilar collaborations Ireland limited unit 35/36 Grange parade, baldoyle industrial estate, Dublin 13, Ireland D13 R20R.
Applied Indication(s):	- First line treatment of adult patients with metastatic carcinoma of the colon or rectum. (In combination with fluoropyrimidine based chemotherapy). - First line treatment of adult patients with metastatic breast cancer. (In combination with paclitaxel). - First line treatment of adult patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxane or anthracycline - containing regimens is not considered appropriate excluding patients who have received taxane and anthracycline-containing regimens in the adjuvant setting within the last 12 months (in combination with capecitabine) - First-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology. (In combination with platinum-based chemotherapy) - First line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer EGFR activating mutations (In combination with Erlotinib) - Indicated for first line treatment of adult patients with advanced and/or metastatic renal cell cancer. (In combination with interferon alfa- 2a) - Front line treatment of adult patients with advanced (FIGO) stage III B, III C and IV epithelial ovarian, fallopian tube or primary peritoneal cancer (In combination with carboplatin & paclitaxel)

	- Treatment of adult patients with first recurrence of platinum- sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-target agents. (In combination with carboplatin & gemcitabine or with carboplatin and paclitaxel) - Treatment of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens and who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-target agents (In combination with paclitaxel, topotecan, or pegylated liposomal doxorubicin). - Treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix. (In combination with paclitaxel & cisplatin or, alternatively paclitaxel & topotecan in patients who cannot receive platinum therapy).
Pharmaceutical form(s) and strength(s):	-Concentrate for solution for Infusion -Strength:25gm/ml
Route of administration	I.V infusion
Approved pack	Abevmy 100 mg (25 mg/ml): 100 mg/4 ml pack of 1 vial (4ml), Single use vial, single unit package, is filled in a 6 ml USP type I glass vial, plugged with a 20mm flurotec chlorobutyl serum rubber stopper and the rubber stopper are latex free, and sealed with a flip-off seal of aluminum and plastic polypropylene. Abevmy 400 mg (25 mg/ml): 400 mg/16 ml pack of 1 vial (16ml), Single use vial, single unit package, is filled in a 20 ml USP type I glass vial, plugged with a 20mm flurotec chlorobutyl serum rubber stopper and the rubber stopper are latex free, and sealed with a flip-off seal of aluminum and plastic polypropylene.

List of abbreviations

ADCC	Antibody dependent cellular cytotoxicity
AS	Active substance
CDC	complement-dependent cytotoxicity
EMA	European medicines agency
FIGO	International Federation of Gynecology and Obstetrics

FP	Finished product
HUVEC	Human Umbilical Vein Endothelial Cells
I.V	intravenous
NSCLC	non-squamous non-small cell lung cancer
VEGF	vascular endothelial growth factor
VEGFR	vascular endothelial growth factor receptor
EGFR	Epidermal growth factor receptor
CHF	Congestive heart failure
mCRC	Metastatic carcinoma of the colon or rectum
mBC	Metastatic breast cancer
PRES	Posterior reversible encephalopathy syndrome
ONJ	Osteonecrosis of the jaw

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance level 1
- The dossier was initially received by the registration administration units on 8.5.2023 after providing all the required documents according to Preliminary checklist (EMA list of questions and answers 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:**

-The active substance of Abevmy (MYL-1402O) has been developed by Mylan as a proposed biosimilar product to the reference medicinal product Avastin having bevacizumab as the active substance.

-The finished product (FP) is a sterile, preservative-free clear to slightly opalescent, colourless to pale brown concentrate for solution for infusion in a single dose vial for intravenous use containing 25 mg/mL of bevacizumab as active substance and is supplied in the market in two presentations: 100 mg/ 4 mL and 400 mg/ 16 mL single-use vials.

-Other ingredients are: α,α-trehalose dihydrate, sodium phosphate (E339), polysorbate 20 (E432) and water for injections

- The product is available in Type I glass vials closed with a flurotec coated, chlorobutyl rubber stopper and sealed with an aluminium seal with plastic flip-off cap.

-Bevacizumab AS (also referred to as MYL-1402O) is a recombinant humanised IgG1 humanised monoclonal antibody which selectively binds to vascular endothelial growth factor (VEGF) and prevents the interaction of VEGF to its receptors (VEGFR-1 and VEGFR-2) on the surface of endothelial cells, thus inhibiting endothelial cell proliferation, angiogenesis, and VEGF-induced vascular permeability.

-Abevmy is intended for the treatment of carcinoma of the colon or rectum, breast cancer, non-small cell lung cancer, renal cell cancer, epithelial ovarian, fallopian tube or primary peritoneal cancer, and carcinoma of the cervix

2. **Quality aspects:**

- **Manufacturer(s):**
  The active substance and drug product manufacture and quality control testing are performed at Biocon Biologics Limited Special Economic Zone, Bengaluru, Karnataka – 560099- India

- **Stability**
  Drug substance:
  Approved Shelf Life: 36 months
  Approved storage Conditions: -20°C ± 5 °C
  Drug product:
  Approved Shelf Life: 30 Months
  Approved Storage Conditions:
- Store in refrigerator (2-8 ◦C).
- Do not freeze
- Keep the vial in the outer carton in order to protect from light
- Do not shake the vial

3. Non-clinical and clinical aspects:

-The results of the in vitro similarity assessment, as well as the single and repeated dose toxicological data, support the demonstration of biosimilarity between Abevmy and the reference drug Avastin.

-In conclusion the overall benefit/risk of Abevmy 100,400 is favorable in the treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer ,unresectable advanced, metastatic or recurrent non-small cell lung cancer , advanced and/or metastatic renal cell cancer , epithelial ovarian, ,fallopian tube or primary peritoneal cancer, persistent, recurrent, or metastatic carcinoma of the cervix.

- **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/abevmy-epar-public-assessment-report_en.pdf