EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Alymsys

Date: October 2024

Unit: Technical Assessment Unit

Assessment report

Alymsys

Administrative information:

Trade name of the medicinal product:	Alymsys 100 mg /4 ml Alymsys 400 mg /16 ml
INN (or common name) of the active substance(s):	Bevacizumab 25 mg/ml
Manufacturer of the finished product	UNIVERSAL FARMA S.L, C/Del Tejido, 2 Azuqueca de Henares , 19200 Guadalajara Spain
Marketing Authorization holder	Mabxience Research SL.C/MANUEL POMBO Angulo 28-3a y 4a planta, 28050 Madrid -Spain
Applied Indication(s):	adult patients with 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, advanced epithelial ovarian, fallopian tube or primary peritoneal cancer and persistent, recurrent, or metastatic carcinoma of the cervix.
Pharmaceutical form(s) and strength(s):	Sterile, preservative-free concentrate for solution for infusion containing 25 mg/mL of bevacizumab as active substance and supplied in two presentations: MB02 100 mg/4 mL and MB02 400 mg/16 mL single-use vials.

Route of administration:	intravenous (IV) infusion
Approved Pack(s):	Carton box containing borosilicate clear Type I glass vial closed with a Type I chlorobutyl rubber stopper coated with fluoropolymer film; flange coated with non-silicone B2 coating and an aluminium seal with a polypropylene yellow flip-off cap with insert leaflet

- **List of abbreviations:**

VEGF	vascular endothelial growth factor
MB02	Bevacizumab
DP	Drug product
EU	Europen union
EPAR	European published assessment report
EGFR	Epidermal Growth Factor Receptor
FIGO	International Federation of Gynecology and Obstetrics

- **Dossier initial submission and evaluation process:**

- The product was submitted for registration via Normal Track (343/2021) pathway.
- The dossier evaluation by the registration administration units was started on 26.3.2023 after providing all the required documents according to the Checklist for documents of new biological products registration file.

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

-Bevacizumab is a recombinant humanised monoclonal antibody that binds specifically to all soluble forms of human vascular endothelial growth factor (VEGF), neutralising its biological activity and acting as an anti-neoplastic agent.

-Bevacizumab MB02 Drug Product (DP) is a proposed biosimilar of Avastin® supplied as a concentrate for solution for infusion at a target concentration of 25 mg/mL.
-The MB02 DP is comparable to the EU-authorised reference medicinal product (Avastin EPAR) in formulation, dosage form (liquid), container closure system, route of administration, and stability.

2. **Quality aspects:**

- **Manufacturer(s):**
  - **Drug substance:**

- Active substance is manufactured at GH GENHELIX S.A Parque technologico de leon- Spain

  - **Drug product:**

-Finished product is manufactured at UNIVERSAL FARMA S.L, C/Del Tejido - Spain

- **Stability**
  - **Drug substance:**

➢ **Approved Storage Conditions of the active substance:**
- Store at -20°C ± 5 °C

➢ **Approved shelf life for the active substance:**
- 36 months

  - **Drug product:**

➢ **Approved Storage Conditions of the finished product:**
- 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
- Chemical and physical in-use stability has been demonstrated for 30 days at 2ºC to 8ºC plus an additional 48 hours at temperature not exceeding 30°C in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally

not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

- **Approved shelf life for the finished product:**
  - 30 months

3. **Non-clinical and clinical aspects:**

-The overall benefit/risk of Alymsys l00mg/4ml & 400mg/16ml is favorable: in combination with fluoropyrimidine-based chemotherapy is indicated for treatment of adult patients with metastatic carcinoma of the colon or rectum.
-Alymsys in combination with paclitaxel is indicated for first-line treatment of adult patients with metastatic breast cancer.
-Alymsys in combination with capecitabine is indicated for first-line treatment of adult patients with metastatic breast cancer in whom treatment with other chemotherapy options including taxanes or anthracyclines is not considered appropriate.
-Patients who have received taxane and anthracycline containing regimens in the adjuvant setting within the last 12 months should be excluded from treatment with Alymsys in combination with capecitabine.
-Alymsys, in addition to platinum-based chemotherapy, is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology.
-Alymsys, in combination with erlotinib, is indicated for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer with Epidermal Growth Factor Receptor (EGFR) activating mutations.
-Alymsys in combination with interferon alfa-2a is indicated for first-line treatment of adult patients with advanced and/or metastatic renal cell cancer.
-Alymsys, in combination with carboplatin and paclitaxel is indicated for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.
-Alymsys, in combination with carboplatin and gemcitabine or in combination with carboplatin and paclitaxel, is indicated for 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-targeted agents.

-Alymsys, in combination with topotecan, or pegylated liposomal doxorubicin is indicated for the 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-targeted agents.
-Alymsys, in combination with paclitaxel and cisplatin or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, is indicated for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix.
-The indications approved for the reference product Avastin were applied for Alymsys except for one concerning platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.
-In case of Avastin (Bevacizumab in combination with paclitaxel, topotecan, or pegylated liposomal doxorubicin is indicated for the 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‑targeted agents) and in Alymsys (in combination with topotecan, or pegylated liposomal doxorubicin is indicated for the 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-targeted agents).

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

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