EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Mylotarg

Date: November 2024

Unit: Technical Assessment Unit

Assessment report

Mylotarg

Administrative information:

Trade name of the medicinal product:	Mylotarg
INN (or common name) of the active substance(s):	Gemtuzumab Ozogamicin 4.5 mg
Manufacturer of the finished product	Wyeth Pharmaceutical Division of Wyeth Holdings LLC, 401 North Middletown Road, Pearl River, NY 10965, United States of America.
Marketing Authorization holder	Wyeth Pharmaceuticals LLC, P.O. Box 8299, Philadelphia, PA 19101, United States of America.
Applied Indication(s):	1.Newly-Diagnosed CD33-positive Acute Myeloid Leukemia (AML) Mylotarg® is indicated for treatment of newly-diagnosed CD33-positive acute myeloid leukemia in adult and pediatric patients 1 month and older. 2.Relapsed or Refactory CD33-positive AML Mylotarg® is indicated for treatment of relapsed or refectory CD33-positive acute myeloid leukemia in adults and pediatric patients 2 years and older.
Pharmaceutical form(s) and strength(s):	- Powder for concentrate for solution for

	infusion (powder for concentrate) - strength: 4.5 mg/vial
Route of administration	-Intravenous (IV) administration
Approved pack	Carton box containing one glass vial of Amber Type 1 borosilicate glass and has a 20 ml nominal fill volume containing 4.5 mg lyophilized powder, closed with a rubber stopper of 20 mm lyophilization design constructed of butyl elastomer and treated with a fluoropolymer film, Sealed with a 20 mm aluminum design with a flip-of cap. With an insert leaflet.

List of abbreviations:

ADC	antibody drug conjugate
AML	Acute Myeloid Leukemia
APL	acute promyelocytic leukemia
AraC	cytarabine
AS	Active substance
EMA	European medicines Agency
FDA	Food and Drug Administration
GO	gemtuzumab ozogamicin (Mylotarg)
IgG	Immunoglobulin G
IV	Intravenous
PK	pharmacokinetic(s)

Dossier initial submission and evaluation process:

- The product was submitted for registration via reliance level II.
- The dossier evaluation by the registration administration units was started on 26.11.2023 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**:

-Gemtuzumab ozogamicin (AS of Mylotarg) is an antibody drug conjugate (ADC) of humanized CD33-directed monoclonal IgG4 antibody covalently bonded to the activated calicheamicin derivative, a semi-synthetic derivative of gamma calicheamicin.

-Gemtuzumab is a drug substance intermediate and is a recombinant, humanized monoclonal antibody (IgG4 with kappa light chains) that binds to the CD33 antigen expressed on the surface of leukemic cells that selectively binds to target antigen, human CD33, and causes Cytotoxicity.
-The total calicheamicin derivative is 24-35 µg/mg protein.

- The finished product is presented as powder for concentrate for solution for infusion containing 5 mg of gemtuzumab ozogamicin as active substance. After reconstitution, the solution contains 1 mg gemtuzumab ozogamicin per mL. Other ingredients are: dextran 40, sucrose, sodium chloride, sodium dihydrogen phosphate monohydrate and disodium hydrogen phosphate anhydrous.

- Mylotarg® is indicated for treatment of newly-diagnosed CD33-positive acute myeloid leukemia in adult and pediatric patients 1 month and older and treatment of relapsed or refectory CD33-positive acute myeloid leukemia in adults and pediatric patients 2 years and older.

2. **Quality aspects:**

- **Manufacturer(s):**

The drug substance and drug product are manufactured and controlled at Wyeth Pharmaceutical Division of Wyeth Holdings LLC, 401 North Middletown Road, Pearl River, NY 10965, United States of America.

- **Stability**

Drug substance:

- **Approved Storage Conditions: 5°C ± 3°C.**
- **Approved shelf life: 1 week**

Drug product:

- **Approved Storage Conditions:** - Refrigerate (2- 8°C)

-Store in the original carton to protect from light.
- Do not freeze.
-Reconstitute each vial with 5 mL of Sterile Water for Injection, USP to obtain a concentration of 1 mg/mL of Mylotarg® that delivers 4.5 mL (4.5 mg**).**
-If the reconstituted solution cannot be used immediately, it may be stored in the original vial for up to16 hours in a refrigerator (2°C to 8°C; 36°F to 46°F) or up to 3 hours at room temperature (up to 30°C). Protect from light. Do not freeze**.**

- **Approved shelf life:** 60 Months

3. Non-clinical and clinical aspects:

- Overall, the non-clinical documentation submitted was considered adequate. The relevant information has been included in the SmPC.
- In conclusion the safety profile of gemtuzumab ozogamicin is considered acceptable, with haemorrhage and infection being the most common adverse reactions (> 30%) in the combination therapy.

For more information, please visit EMA published assessment report link:
https://www.ema.europa.eu/en/documents/assessment-report/mylotarg-epar-public-assessment-report_en.pdf