Clinical Policy: Gemtuzumab Ozogamicin (Mylotarg)

Reference Number: PA.CP.PHAR.358
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Revision Log

Description
Gemtuzumab ozogamicin (Mylotarg™) is a CD33 directed antibody-drug conjugate.

FDA Approved Indication(s)
Mylotarg is indicated for the treatment of:

- Newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults
- Relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with PA Health & Wellness that Mylotarg is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of CD33-positive AML;
2. Member meets a or b:
   a. Age ≥ 18 years with newly-diagnosed disease;
   b. Age ≥ 2 years with relapsed or refractory disease;
3. Dose does not exceed the FDA-approved dose and schedule (*see Section V*).

Approval duration: 12 months (*Up to a total of 10 doses*)

B. Acute Promyelocytic Leukemia (off-label) (must meet all):

1. Diagnosis of acute promyelocytic leukemia;
2. Member is not in remission following treatment for relapsed disease (e.g., arsenic trioxide, all-trans retinoic acid, idarubicin);
3. Request meets one of the following (a or b):
   1. Dose does not exceed the FDA approved dose and schedule (see Section V);
   2. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months (Up to 10 doses)

C. Other diagnoses/indications

1. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., no significant toxicity);
3. Member has NOT received the maximum treatment cycles recommended as described below (a, b or c):
   a. In combination with daunorubicin and cytarabine for newly diagnosed AML: up to 5 doses;
   b. As single agent for newly diagnosed AML: up to 10 doses;
   c. Relapse or refractory AML: up to 3 doses;
4. If request is for a dose increase, new dose does not exceed the FDA approved dose and schedule (*see Section V*).

Approval duration: 12 months *(Approve requested number of doses required to complete therapy and not to exceed a total of 10 doses)*

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
AML: acute myeloid leukemia
FDA: Food and Drug Administration

Appendix B: General Information
- Mylotarg originally received accelerated approval in May 2000 as a stand-alone treatment for older patients with CD33-positive AML who had experienced a relapse. Mylotarg was voluntarily withdrawn from the market after subsequent confirmatory trials failed to verify clinical benefit and demonstrated safety concerns, including a high number of fatal induction adverse events. The recent FDA approval is at a lower dose (previously 9 mg/m^2) and different treatment schedule.
- Mylotarg prescribing information includes a black box warning related to hepatotoxicity, including severe or fatal hepatic veno-occlusive disease, also known as sinusoidal obstruction syndrome, associated with the use of Mylotarg.
- Refer to prescribing information for dose modifications for hematologic and nonhematologic toxicities.

- NCCN treatment guidelines for AML recommend (Category 2A) Mylotarg be considered on a compassionate use basis for acute promyelocytic leukemia in patients not in remission after receiving therapy for first disease relapse.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML newly-diagnosed (combination regimen)	*Induction:* 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine. If a second induction cycle is required, do NOT administer Mylotarg. *Consolidation:* 3 mg/m^2 on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine for two cycles.	4.5 mg/dose (for one induction and two consolidation cycles)
AML newly-diagnosed (single-agent regimen)	*Induction:* 6 mg/m^2 on Day 1 and 3 mg/m^2 on Day 8 *Continuation:* For patients without evidence of disease progression following induction, up to 8 continuation courses of Mylotarg 2 mg/m^2 on Day 1 every 4 weeks	Maintenance: 2 mg/m^2 every 4 weeks for up to 8 doses
AML relapsed or refractory (single-agent regimen)	3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7	4.5 mg/dose

VI. Product Availability

Injection: 4.5 mg as a lyophilized cake or powder in a single-dose vial

VII. References

1. Mylotarg Prescribing Information. Wyeth Pharmaceuticals Inc.; Philadelphia, PA. September 2017. Available at: www.mylotarg.com. Accessed September 11, 2017.
2. NCCN Guidelines: Acute Myeloid Leukemia. Version 3.2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed September 11, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created	07/18/18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01/01/2020	07/17/19	