Clinical Policy: Gemtuzumab Ozogamicin (Mylotarg)

Reference Number: ERX.SPA.351
Effective Date: 12.01.19
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 and pediatric patients 1 month and older
- Relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Prescribed by or in consultation with an oncologist or hematologist;
3. Member meets (a or b):
   a. Age ≥ 1 month with newly diagnosed disease;
   b. Age ≥ 2 years with relapsed or refractory disease;
4. Request meets one of the following (a, b, c, d, or e):*
   a. Age 1 month to < 18 years: Newly diagnosed disease as combination therapy with standard chemotherapy (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (body surface area [BSA] < 0.6 m^2) or 3 mg/m^2 (BSA ≥ 0.6 m^2) given once;
      ii. Intensification - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (BSA < 0.6 m^2) or 3 mg/m^2 (BSA ≥ 0.6 m^2) given once;
   b. Age ≥ 18 years: Newly diagnosed disease as combination therapy with daunorubicin and cytarabine (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 3 mg/m^2 on Days 1, 4, and 7;
      ii. Consolidation - 2 cycles (2 vials): dose does not exceed 3 mg/m^2 on Day 1 of each cycle;
   c. Age ≥ 18 years: Newly diagnosed disease as single-agent therapy (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 6 mg/m^2 on Day 1, and 3 mg/m^2 on Day 8;
      ii. Continuation therapy - 8 cycles (8 vials): dose does not exceed 2 mg/m^2 on Day 1 of each cycle;
   d. Age ≥ 2 years: Relapsed or refractory disease (single-agent regimen): single course: dose does not exceed 3 mg/m^2 on Days 1, 4, and 7 (3 vials);

e. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Mylotarg for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For AML, member has NOT received the maximum treatment cycles recommended as described below (a, b, or c):
   a. As combination therapy with daunorubicin and cytarabine for newly diagnosed disease: up to 5 doses;
   b. As single-agent therapy for newly diagnosed disease: up to 10 doses;
   c. As single-agent therapy for relapsed or refractory disease: up to 3 doses;
4. If request is for a dose increase, request meets one of the following (a, b, c, d, or e):*
   a. Age 1 month to < 18 years: Newly diagnosed disease as combination therapy with standard chemotherapy (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (body surface area [BSA] < 0.6 m^2) or 3 mg/m^2 (BSA ≥ 0.6 m^2) given once;
      ii. Intensification - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (BSA < 0.6 m^2) or 3 mg/m^2 (BSA ≥ 0.6 m^2) given once;
   b. Age ≥ 18 years: Newly diagnosed disease as combination therapy with daunorubicin and cytarabine (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 3 mg/m^2 on Days 1, 4, and 7;
      ii. Consolidation - 2 cycles (2 vials): dose does not exceed 3 mg/m^2 on Day 1 of each cycle;
   c. Age ≥ 18 years: Newly diagnosed disease as single-agent therapy (i and ii):
      i. Induction - 1 cycle (1 vial): dose does not exceed 6 mg/m^2 on Day 1, and 3 mg/m^2 on Day 8;
      ii. Continuation therapy - 8 cycles (8 vials): dose does not exceed 2 mg/m^2 on Day 1 of each cycle;
   d. Age ≥ 2 years: Relapsed or refractory disease (single-agent regimen): single course: dose does not exceed 3 mg/m^2 on Days 1, 4, and 7 (3 vials);
   e. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
AML: acute myeloid leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Center

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): hypersensitivity
- Boxed warning(s): hepatotoxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML newly-diagnosed (combination regimen)	Adults: *Induction:* 3 mg/m^2 IV (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 IV on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine for 2 cycles. Pediatric patients > 1 month: 3 mg/m^2 IV with body surface area (BSA) > 0.6 m^2. 0.1 mg/kg with body surface area (BSA) < 0.6 m^2	*Induction:* 4.5 mg/dose (1 cycle) *Consolidation:* 4.5 mg/dose (2 cycles) *Induction pediatric*: 1 cycle *Consolidation pediatric*: 1 cycle
AML newly-diagnosed (single-agent regimen)	Adults: *Induction:* 6 mg/m^2 IV on Day 1 and 3 mg/m^2 on Day 8 for 1 cycle *Continuation:* 2 mg/m^2 IV on Day 1 every 4 weeks for up to 8 cycles	*Induction:* 6 mg/m^2/dose (1 cycle) *Maintenance:* 2 mg/m^2/dose every 4 weeks (8 cycles)
AML relapsed or refractory (single-agent regimen)	Age 2 years and older: 3 mg/m^2 IV (up to one 4.5 mg vial) on Days 1, 4, and 7 for 1 cycle	4.5 mg/dose (1 cycle)

VI. Product Availability

Single-dose vial: 4.5 mg

VII. References

1. Mylotarg Prescribing Information. Wyeth Pharmaceuticals Inc.; Philadelphia, PA. June 2020. Available at: https://www.pfizerpro.com/product/mylotarg. Accessed August 11, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 14, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 14, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	08.20.19	11.19
4Q 2020 annual review: no significant changes; updated age limit to 1 month from 18 years for newly diagnosed AML as per FDA label; references reviewed and updated.	08.15.20	11.20
4Q 2021 annual review: updated age limit for acute promyelocytic leukemia as per NCCN; updated section V dosing; references reviewed and updated.	08.11.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.