Clinical Policy: Gemtuzumab Ozogamicin (Mylotarg)

Reference Number: CP.PHAR.358
Effective Date: 10.03.17
Last Review Date: 11.17
Line of Business: 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
- 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 Centene Corporation® 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 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 Centene benefit, or documentation supports that member is currently receiving Mylotarg for AML;
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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to 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 – 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
Policy created	10.03.17	11.17

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.