Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Gemtuzumab ozogamicin (Mylotarg®)	MP-RX-FP-62-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description

This document addresses the use of Gemtuzumab ozogamicin (Mylotarg), a CD33-directed antibody and cytotoxic drug conjugate approved by the Food and Drug Administration (FDA) for the treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) and relapsed or refractory CD33-positive AML.

Background Information

Originally FDA approved in 2000, Mylotarg was subsequently voluntarily withdrawn from the US market in 2010 due to safety and efficacy concerns. A required post-marketing study of the addition of Mylotarg to standard induction as first-line therapy for AML in individuals < 61 years of age showed significantly greater fatal induction toxicity and no improvement in survival compared to chemotherapy alone (NCT00085709; Petersdorf 2013). Re-approval for Mylotarg in 2017 was granted based on studies showing event- free survival advantage, overall survival advantage, or durable complete remission (Castaigne 2012, Amadori 2016, Hills 2014). The FDA approved indications include treatment of newly diagnosed AML (including induction and consolidation [post-remission] therapy) and treatment of relapsed or refractory AML.

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Mylotarg. These include the use in high-risk acute promyelocytic leukemia (APL). NCCN identifies APL as high risk when white blood count (WBC) is greater than 10,000/mcL (cells per microliter). While NCCN includes a recommendation for Mylotarg in low- risk APL individuals if arsenic is not available or contraindicated, there is a lack of high-quality data to support this use.

Mylotarg has a black box warning for hepatotoxicity, including severe or fatal hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS) which has been reported within single agent and combination therapy. Individuals should be monitored frequently for signs and symptoms of VOD.

Definitions and Measures

- Acute promyelocytic leukemia (APL): an aggressive subtype of AML
- Anthracycline: A type of antibiotic that comes from certain types of Streptomyces bacteria and are used to treat many types of cancer. Anthracyclines damage the DNA in cancer cells, causing the cells to die.
- Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.
- Refractory Disease: Illness or disease that does not respond to treatment.

Policy Name	Policy Number	Scope
Gemtuzumab ozogamicin (Mylotarg®)	MP-RX-FP-62-23	☒ MMM MA ☒ MMM Multihealth

- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Approved Indications

Mylotarg is approved by the FDA for:

- Adults and pediatric patients 1 month and older with newly diagnosed CD33-positive acute myeloid leukemia (AML).
- Adults and pediatric patients 2 years and older with relapsed or refractory CD33-positive AML.

Other Uses

See Background section above.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9203	Injection, gemtuzumab ozogamicin, 0.1 mg [Mylotarg]

ICD-10	Description
C92.00-C92.02	Acute myeloblastic leukemia
C92.40-C92.42	Acute promyelocytic leukemia
C92.50-C92.52	Acute myelomonocytic leukemia
C92.60-C92.62	Acute myeloid leukemia with 11q23-abnormality
C92.A0-C92.A2	Acute myeloid leukemia with multilineage dysplasia
C93.00-C93.02	Acute monoblastic/monocytic leukemia
C94.00-C94.02	Acute erythroid leukemia
C94.20-C94.22	Acute megakaryoblastic leukemia

Policy Name	Policy Number	Scope
Gemtuzumab ozogamicin (Mylotarg®)	MP-RX-FP-62-23	☒ MMM MA ☒ MMM Multihealth

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

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

Gemtuzumab ozogamicin (Mylotarg®)

A. Criteria For Initial Approval

i. Individual has a diagnosis of CD33+ acute myeloid leukemia (AML); **AND**

ii. Individual is using for one of the following:

A. As induction for AML; **OR**

B. As consolidation therapy for AML; **OR**

C. As treatment for relapsed or refractory AML;

OR

iii. Individual has a diagnosis of acute promyelocytic leukemia (APL) (NCCN 2A); **AND**

A. Individual has high-risk disease.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Gemtuzumab ozogamicin (Mylotarg®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen, and the maximum duration of treatment has not been exceeded. The following information should be submitted for reauthorization:

A. A current oncology note documenting the patient's response to treatment showing no progression of disease.

B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

ii. Maximum Duration of Therapy:

A. Newly-Diagnosed De Novo CD33-positive AML (Combination Regimen): 1 induction cycle and 2 consolidation cycles.

B. Newly-Diagnosed CD33-positive AML (Single-agent Regimen): 1 induction cycle and 8 consolidation cycles.

C. Relapsed or Refractory CD33-positive AML (Single-agent Regimen): 1 single course

C. Authorization Duration

i. Initial Approval Duration: Per cycle or course

ii. Reauthorization Approval Duration: Per cycle or course

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Mylotarg (gemtuzumab ozogamicin) may not be approved if the above criteria are not met and for all other indications.

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Policy Name	Policy Number	Scope
Gemtuzumab ozogamicin (Mylotarg®)	MP-RX-FP-62-23	☒ MMM MA ☒ MMM Multihealth

Indication	Recommended Treatment Regimen	Recommended Dosing Schedule
Newly-Diagnosed De Novo CD33-positive AML (Combination Regimen)	1 induction cycle and 2 consolidation cycles	Induction Cycle: 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine. In patients needing a second induction cycle, Mylotarg should not be administered. Consolidation Cycles: 3 mg/m^2 on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine
Newly-Diagnosed CD33-positive AML (Single-agent Regimen)	1 cycle of induction and up to 8 cycles of continuation therapy	Induction Cycle: 6 mg/m^2 (not limited to one 4.5 mg vial) as a single agent on Day 1, and 3 mg/m^2 (not limited to one 4.5 mg vial) on Day 8. Consolidation Cycles: 2 mg/m^2 (not limited to one 4.5 mg vial) as a single agent on Day 1 every 4 weeks.
Relapsed or Refractory CD33-positive AML (Single-agent Regimen)	One single course	3 mg/m2 (up to one 4.5 mg vial) on Days 1, 4, and 7
Exceptions		
None		

Reference Information

1. Abaza Y, Kantarjian H, Garcia-Manero G, et al. Long-term outcome of acute promyelocytic leukemia treated with all-trans-retinoic acid, arsenic trioxide, and gemtuzumab. Blood. 2017; 129(10):1275-1283.
2. Amadori S, Suciu S, Selleslag D, et al. Gemtuzumab ozogamicin versus best supportive care in older patients with newly diagnosed acute myeloid leukemia unsuitable for intensive chemotherapy: results of the randomized phase III EORTC-GIMEMA AML-19 trial. J Clin Oncol. 2016; 34(9):972-979
3. Burnett AK, Hills RK, Milligan D, et al. Identification of patients with acute myeloblastic leukemia who benefit from the addition of gemtuzumab ozogamicin: results of the MRC AML 15 trial. J Clin Oncol 2011; 29:369-377.
4. Burnett AK, Russell NH, Hills RK, et al. Arsenic trioxide and all-trans retinoic acid treatment for acute promyelocytic leukaemia in all risk groups (AML17): results of a randomised, controlled, phase 3 trial. Lancet Oncol. 2015;16(13):1295-1305.

5. Castaigne S, Pautas C, Terré C, et al; Acute Leukemia French Association. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012; 379(9825):1508-1516.
6. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 20, 2023.
7. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
8. Hills RK, Castaigne S, Appelbaum FR, et al. Addition of gemtuzumab ozogamicin to induction chemotherapy in adult patients with acute myeloid leukaemia: a meta-analysis of individual patient data from randomised controlled trials. Lancet Oncol. 2014; 15(9):986-996.
9. Lambert J, Pautas C, Terré C et al. Gemtuzumab ozogamicin for de novo acute myeloid leukemia: final efficacy and safety updates from the open-label, phase 3 ALFA-0701 trial. Haematologica. 2018 Aug 3; Epub ahead of print.
10. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
11. Southwest Oncology Group. A phase III study of the addition of gemtuzumab ozogamicin (Mylotarg®) during induction therapy versus standard induction with daunomycin and cytosine arabinoside followed by consolidation and subsequent randomization to post-consolidation therapy with gemtuzumab ozogamicin (Mylotarg®) or no additional therapy for patients under age 61 with previously untreated de novo acute myeloid leukemia (AML). NLM Identifier: NCT00085709; SWOG Identifier S0106. Last updated on September 25, 2015. Available at: https://clinicaltrials.gov/ct2/show/results/NCT00085709. Accessed on March 22, 2019.
12. Petersdorf SH, Kopecky KJ, Slovak M, et al. A phase 3 study of gemtuzumab ozogamicin during induction and postconsolidation therapy in younger patients with acute myeloid leukemia. Blood. 2013; 121(24):4854-4860.
13. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 20, 2023.
    a. Acute Myeloid Leukemia. V3.2022. Revised January 13, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy Name	Policy Number	Scope
Gemtuzumab ozogamicin (Mylotarg®)	MP-RX-FP-62-23	☒ MMM MA ☒ MMM Multihealth

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 11/19/2023