Clinical Criteria

Subject:	Mylotarg (gemtuzumab ozogamicin)		
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Overview

This document addresses the use of Mylotarg (gemtuzumab ozogamicin). Mylotarg is an antibody-drug conjugate composed of a monoclonal antibody targeting CD33 and the cytotoxic agent of calicheamicin, which is released into the malignant cells upon binding. It is used to treat acute myeloid leukemia (AML).

Originally FDA approved in 2000, Mylotarg was subsequently voluntarily withdrawn from the US market in 2010 due to safety and efficacy concerns.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). NCCN previously recommended Mylotarg only in patients who were unable to tolerate anthracycline-based therapy. In 2018, NCCN updated the high-risk APL algorithm to include Mylotarg as a preferred regimen alongside anthracycline-based regimens with no preference for one over the other. This recommendation cites one retrospective uncontrolled study (Abaza 2017) which showed a similar 5-year overall survival between those who received Mylotarg and those who received idarubicin (an anthracycline).

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.

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.

Clinical Criteria

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.

Mylotarg (gemtuzumab ozogamicin)

Requests for Mylotarg (gemtuzumab ozogamicin) may be approved if the following criteria are met:

I. Individual has a diagnosis of CD33+ acute myeloid leukemia (AML); **AND**
II. Individual is using for one of the following:
    A. Newly-diagnosed AML; **OR**
    B. Relapsed or refractory AML;

OR
III. Individual has a diagnosis of acute promyelocytic leukemia (APL) (NCCN 2A); **AND**
    A. Individual has high-risk disease; **AND**
    B. Individual is ineligible for treatment with an anthracycline.

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

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9203	Injection, gemtuzumab ozogamicin, 0.1 mg [Mylotarg]

ICD-10 Diagnosis

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

Document History

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- 02/25/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: No changes. Coding Reviewed: No changes.
- 08/21/2020– Select Review: Remove age from criteria. Coding review: No changes.
- 02/21/2020– Annual Review: Formatting change. Coding Reviewed: No changes
- 05/17/2019– Annual Review: First review of Mylotarg clinical criteria. Minor wording and formatting updates. Add reference for off label criteria. Coding reviewed: No changes.

References

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. 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.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
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 14, 2022.
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.; 2022; 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™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 14, 2022.
    a. Acute Myeloid Leukemia. V1.2022. Revised December 2, 2021.

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.