



POLICY NUMBER UM_1325	SUBJECT Mylotarg™ (gemtuzumab ozogamicin)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATE REVIEWED 09/13/17, 09/04/18, 08/08/19	APPROVAL DATE August 14, 2019	EFFECTIVE DATE August 14, 2019	REVISION DATES (latest version listed last) 09/13/17, 09/21/18, 08/14/19	
PRIMARY BUSINESS OWNER: APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Oncology	

I. PURPOSE

To define and describe the accepted indications for Mylotarg (gemtuzumab ozogamicin) usage in the treatment of cancer.

II. DEFINITIONS

Mylotarg (gemtuzumab ozogamicin): is a CD33-directed antibody-drug conjugate. The cytotoxic agent is a small molecule, N-acetyl gamma calicheamicin, and the antibody portion, hP67.6, recognizes human CD33 antigen. Gemtuzumab ozogamicin binds to the CD33 antigen expressed by hematopoietic cells which forms a complex that is internalized by the tumor cell. Once internalized, the calicheamicin derivative is released and activated, causing DNA double-strand breaks, cell cycle arrest, and apoptotic cell death.

Mylotarg (gemtuzumab ozogamicin) is FDA approved for the treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults and for treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older. Gemtuzumab ozogamicin may be used in combination with daunorubicin and cytarabine for adults with newly-diagnosed AML, or as a stand-alone treatment for certain adult and pediatric patients. Compared to the original labeling, the current FDA approval includes a lower recommended dose, a different schedule in combination with chemotherapy or on its own, and a new patient population.

Mylotarg (gemtuzumab ozogamicin) is available in 4.5 mg as a lyophilized cake or powder in a single-dose vial for reconstitution and dilution.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Mylotarg (gemtuzumab ozogamicin) may be considered medically necessary when any of the following selection criteria is met:

1. Acute Myeloid Leukemia (AML)

- a. The member has CD33-positive AML and Gemtuzumab ozogamicin is being used for ONE of the following criteria:



- i. In combination with daunorubicin and cytarabine for members <60 years of age with new diagnosed AML (treatment naive)
- ii. As a single agent for members not eligible for intensive chemotherapy, ≥60 years of age, for newly diagnosed or relapsed/refractory AML.

2. Acute Promyelocytic Leukemia

- a. The member has high-risk APL (white blood cell count >10,000/mcL) and Mylotarg (gemtuzumab ozogamicin) is being used as **ONE** of the following:
 - i. Induction therapy in combination with tretinoin (ATRA) +/- arsenic trioxide **OR**
 - ii. Consolidation therapy in combination with tretinoin (ATRA) or arsenic trioxide if tolerated **OR**
 - iii. Relapsed or refractory therapy in combination arsenic trioxide +/- tretinoin (ATRA).

Exclusion Criteria: Mylotarg (gemtuzumab ozogamicin) is not considered medically necessary when any of the following selection criteria is met:

- 1. Mylotarg (gemtuzumab ozogamicin) is being used after disease progression with the same regimen.
- 2. Dosing exceeds single dose limit of Mylotarg (gemtuzumab ozogamicin) combination therapy 3mg/m² (max dose is 4.5 mg) or 6 mg/m² as single agent.
- 3. Treatment exceeds the maximum duration limit of 8 cycles of induction therapy.
- 4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Mylotarg (gemtuzumab ozogamicin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. Dosage and Administration

- a. Newly diagnosed AML:
 - i. Prior to initiation (Patients with leukocyte count $30 \times 10^9/L$ [i.e., 30 giga (Gi)/L or greater]), cytoreduction recommended
 - ii. Premedication, acetaminophen 650 mg orally and diphenhydramine 50 mg orally/IV administered 1 hour prior to gemtuzumab ozogamicin and methylprednisolone 1 mg/kg or equivalent dose of other corticosteroid within 30 minutes prior to infusion
 - iii. Induction cycle (Combination regimen), 3 mg/m² IV infusion over 2 hours on days 1, 4, and 7 in combination with Daunorubicin 60 mg/m² on days 1 to 3 and cytarabine 200 mg/m² on days 1 to 7; Max one 4.5 mg vial; may administer a second chemotherapy induction cycle without gemtuzumab ozogamicin
 - iv. First consolidation cycle (Combination regimen), 3 mg/m² IV infusion over 2 hours on day 1 in combination with Daunorubicin 60 mg/m² IV on day 1 and cytarabine 1 g/m² IV every 12 hours on days 1 to 4; Max one 4.5 mg vial



- v. Second consolidation cycle (Combination regimen), 3 mg/m² IV infusion over 2 hours on day 1 in combination with Daunorubicin 60 mg/m² IV on days 1 and 2 and cytarabine 1 g/m² IV every 12 hours on days 1 to 4; Max one 4.5 mg vial
- vi. Induction cycle (Single-agent regimen), 6 mg/m² IV infusion over 2 hours on day 1 and 3 mg/m² on day 8
- vii. Continuation cycle (Single-agent regimen), 2 mg/m² IV infusion over 2 hours on day 1 every 4 weeks; may administer up to 8 cycles of continuation therapy

b. Relapsed or refractory AML:

- i. Prior to initiation (Patients with leukocyte count $30 \times 10^9/L$ [i.e., 30 giga (Gi)/L or greater]), cytoreduction recommended
- ii. Premedication, acetaminophen 650 mg orally and diphenhydramine 50 mg orally/IV administered 1 hour prior to gemtuzumab ozogamicin and methylprednisolone 1 mg/kg or equivalent dose of other corticosteroid within 30 minutes prior to infusion
- iii. 3 mg/m² IV infusion over 2 hours on days 1, 4, and 7; max one 4.5 mg vial

2. **Dosage Adjustments:**

- a. Hepatic tests (Total bilirubin greater than 2 times ULN or AST and/or ALT greater than 2.5 times ULN): Delay treatment until recovery of total bilirubin to 2 times ULN or less and AST and ALT to 2.5 x ULN or less prior to each dose. If dose is delayed more than 2 days between sequential infusions, omit scheduled dose.
- b. Infusion related reactions: Interrupt infusion and treat medically (acetaminophen, diphenhydramine, and/or methylprednisolone). Provide supportive care measures. For mild, moderate, and severe infusions consider resuming infusion at one-half or less of the rate at which the reaction occurred once symptoms resolve. Interrupt the infusion and retreat if symptoms recur.
- c. Infusion related reactions (Severe or life-threatening): Permanently discontinue.
- d. Nonhematologic toxicity (Severe or life-threatening): Delay treatment until recovery of no more than mild. If dose is delayed more than 2 days between sequential infusions, omit scheduled dose.
- e. Persistent neutropenia (Neutrophil count not recovered to 0.5×10^9 [i.e., 0.5 giga (Gi)/L] within 14 days following planned start date of consolidation cycle) in patients receiving combination therapy: Discontinue gemtuzumab ozogamicin treatment; do not administer gemtuzumab ozogamicin in consolidation cycles.
- f. Persistent thrombocytopenia (Platelet count not recovered to 100×10^9 [ie, 100 Gi/L] within 14 days following planned start date of consolidation cycle) in patients receiving combination therapy: Discontinue gemtuzumab ozogamicin treatment; do not administer gemtuzumab ozogamicin in consolidation cycles.

3. **Monitoring**

- a. Resolution or improvement of disease-related signs (reduction of blasts in the bone marrow and peripheral blood, recovery of blood counts, and resolution of extramedullary disease) may indicate efficacy.

- b. ALT, AST, total bilirubin, and alkaline phosphatase: Prior to each dose.
- c. Blood counts: Prior to each dose and frequently after treatment.
- d. Electrolytes, in patients at risk for QT-interval prolongation: Prior to initiation and as clinically indicated thereafter.
- e. Signs and symptoms of veno-occlusive disease: Frequently following treatment.
- f. Vital signs and infusion-related reactions: During infusion and for at least 1 hour after termination.
- g. Signs or symptoms of bleeding
- h. ECG, in patients at risk for QT-interval prolongation: Prior to initiation and as clinically indicated thereafter.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Mylotarg PI prescribing information. Pfizer Inc, Philadelphia, PA 2018.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.