

Clinical Policy: Gemtuzumab Ozogamicin (Mylotarg)

Reference Number: PA.CP.PHAR.358

Effective Date: 10/2017

Last Review Date: 10/2024

Description

Gemtuzumab ozogamicin (Mylotarg™) is a CD33 directed antibody and cytotoxic 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of PA Health & Wellness 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 \geq 1 month with newly diagnosed disease;
 - b. Age \geq 2 years with relapsed or refractory disease;
4. Mylotarg is prescribed as one of the following (a, b, c, d, e or f):
 - a. As combination with chemotherapy for newly diagnosed disease: up to 5 doses;
 - b. As combination therapy with standard chemotherapy (pediatric: 1 month or older) for newly diagnosed disease: up to 2 doses;
 - c. As single-agent therapy for newly diagnosed disease: up to 10 doses;
 - d. As single-agent therapy for relapsed or refractory disease: up to 3 doses;
 - e. As a component of repeating the initial successful induction regimen for relapsed or refractory disease if \geq 12 months since induction regimen: up to 3 doses;
 - f. Other category 1, 2A, or 2B NCCN-recommended uses not listed;
5. 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 m²) or 3 mg/m² (BSA \geq 0.6 m²) given once;

- ii. Intensification - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (BSA < 0.6 m²) or 3 mg/m² (BSA ≥ 0.6 m²) given once;
- b. Age ≥ 18 years: Newly diagnosed disease as combination therapy with daunorubicin and cytarabine (i and ii):
 - i. Induction - 1 cycle (3 vials): dose does not exceed 3 mg/m² on Days 1, 4, and 7;
 - ii. Consolidation - 2 cycles (2 vials): dose does not exceed 3 mg/m² on Day 1 of each cycle;
- c. Age ≥ 18 years: Newly diagnosed disease as single-agent therapy (i and ii):
 - i. Induction - 1 cycle: dose does not exceed 6 mg/m² on Day 1, and 3 mg/m² on Day 8;
 - ii. Continuation therapy - 8 cycles: dose does not exceed 2 mg/m² 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/m² 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*).

Approval duration: 12 months

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*).

Approval duration: 12 months

C. Other diagnoses/indications

- 1. Refer to PA.CP.PHAR.53 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 PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
- 2. Member is responding positively to therapy;
- 3. For AML, member has NOT received the maximum recommended doses as described below (a, b, c, d, e or f):
 - a. As combination with chemotherapy for newly diagnosed disease: up to 5 doses;
 - b. As combination therapy with standard chemotherapy (pediatric: 1 month or older) for newly diagnosed disease: up to 2 doses;
 - c. As single-agent therapy for newly diagnosed disease: up to 10 doses;
 - d. As single-agent therapy for relapsed or refractory disease: up to 3 doses;

- e. As a component of repeating the initial successful induction regimen for relapsed or refractory disease if ≥ 12 months since induction regimen: up to 3 doses;
 - f. For other category 1, 2A, or 2B NCCN-recommended uses not listed (*see Appendix D*), 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;
4. For acute promyelocytic leukemia, 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*).
 5. 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] $< 0.6 \text{ m}^2$) or 3 mg/m² (BSA $\geq 0.6 \text{ m}^2$) given once;
 - ii. Intensification - 1 cycle (1 vial): dose does not exceed 0.1 mg/kg (BSA $< 0.6 \text{ m}^2$) or 3 mg/m² (BSA $\geq 0.6 \text{ m}^2$) given once;
 - b. Age ≥ 18 years: Newly diagnosed disease as combination therapy with daunorubicin and cytarabine (i and ii):
 - i. Induction - 1 cycle (3 vials): dose does not exceed 3 mg/m² on Days 1, 4, and 7;
 - ii. Consolidation - 2 cycles (2 vials): dose does not exceed 3 mg/m² on Day 1 of each cycle;
 - c. Age ≥ 18 years: Newly diagnosed disease as single-agent therapy (i and ii):
 - i. Induction - 1 cycle: dose does not exceed 6 mg/m² on Day 1, and 3 mg/m² on Day 8;
 - ii. Continuation therapy - 8 cycles: dose does not exceed 2 mg/m² 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/m² 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*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies; **Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to PA.CP.PHAR.53 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 – PA.CP.PHAR.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

- AML: acute myeloid leukemia
- BSA: body surface area
- FDA: Food and Drug Administration
- NCCN: National Comprehensive Cancer Center

Appendix B: General Information

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to Mylotarg or any of its components
- Boxed warning(s): hepatotoxicity

Appendix D: Acute Myeloid Leukemia NCCN Recommendations

NCCN recommends Mylotarg in combination with additional agents [e.g., fludarabine, high-dose cytarabine, idarubicin, and granulocyte colony-stimulating factor (G-CSF) OR with high-dose cytarabine for patients age <60 years with NPM1-mutated and FLT3 negative in favorable-risk AML (CBF-AML, NPM1-mutated/FLT3 wild-type AML, in-frame bZIP mutation in CEBPA)].

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML newly-diagnosed (combination regimen)	<p>Adults: <i>Induction:</i> 3 mg/m² 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.</p> <p><i>Consolidation:</i> 3 mg/m² IV on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine for 2 cycles.</p> <p>Pediatric patients > 1 month:</p> <ul style="list-style-type: none"> • BSA ≥ 0.6 m²: 3 mg/m² IV • BSA < 0.6 m² : 0.1 mg/kg IV 	<p><i>Induction:</i> 4.5 mg/dose (1 cycle)</p> <p><i>Consolidation:</i> 4.5 mg/dose (2 cycles)</p> <p><i>Induction pediatric:</i> 1 cycle</p> <p><i>Consolidation pediatric:</i> 1 cycle</p>
AML newly-diagnosed (single-agent regimen)	<p>Adults: <i>Induction:</i> 6 mg/m² IV on Day 1 and 3 mg/m² on Day 8 for 1 cycle</p> <p><i>Continuation:</i> 2 mg/m² IV on Day 1 every 4 weeks for up to 8 cycles</p>	<p><i>Induction:</i> 6 mg/m²/dose (1 cycle)</p> <p><i>Maintenance:</i> 2 mg/m²/dose every 4 weeks (8 cycles)</p>

AML relapsed or refractory (single-agent regimen)	Age \geq 2 years: 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)
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VI. Product Availability

Single-dose vial: 4.5 mg

VII. References

1. Mylotarg Prescribing Information. Wyeth Pharmaceuticals Inc.; Philadelphia, PA. August 2021. Available at <https://www.pfizer.com/products/product-detail/mylotarg>. Accessed July 11, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 15, 2024.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 15, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9203	Injection, gemtuzumab ozogamicin, 0.1 mg

Reviews, Revisions, and Approvals	Date
New policy created	07/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01/01/2020	07/2019
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: for acute promyelocytic leukemia, added age limit and removed requirement for use only for relapse as NCCN compendia include use for induction and consolidation; FDA/NCCN dosage limitations added; updated age limit to 1 month from 18 years for new diagnosed AML as per FDA label; references reviewed and updated	08/2020
4Q 2021 annual review: updated age limit for acute promyelocytic leukemia as per NCCN; updated section V dosing; references reviewed and updated.	10/2021
4Q 2022 annual review: max recommended number of doses removed from approval duration and clarified within section I/II; references reviewed and updated.	10/2022
4Q 2023 annual review: added combination therapy option for relapsed/refractory AML per NCCN-supported off-label use; references reviewed and updated.	10/2023

Reviews, Revisions, and Approvals	Date
4Q 2024 annual review: for AML, collapsed combination therapy options for newly diagnosed disease to “combination with chemotherapy” as there are various recommended combinations per NCCN; references reviewed and updated.	10/2024