Mylotarg™ (gemtuzumab ozogamicin) (Intravenous)

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I. Length of Authorization [1,5-8,11]

Newly-Diagnosed AML

- Initial: Prior authorization validity will be provided initially for 6 months (180 days), unless otherwise specified.
  - In combination with daunorubicin and cytarabine (adult): Prior authorization validity will be provided for 6 months consisting of 3 cycles (1 induction and 2 consolidation).
  - In combination with daunorubicin and cytarabine (pediatric): Prior authorization validity will be provided for 6 months consisting of 2 cycles (1 induction and 1 consolidation).
  - In combination with idarubicin and cytarabine (adult): Prior authorization validity will be provided for 6 months consisting of 3 cycles (1 induction and 2 consolidation).
  - In combination with high-dose cytarabine (adult) as consolidation therapy: Prior authorization validity will be provided for 6 months consisting of 2 cycles (2 doses).
- Renewal: Prior authorization validity may NOT be renewed, unless otherwise specified.
  - Single-agent therapy: Prior authorization validity may be renewed for up to a maximum of 8 cycles of continuation.

Relapsed or Refractory AML

- Initial: Prior authorization validity will be provided initially for 6 months (180 days) consisting of 1 cycle (3 doses).
- Renewal: Prior authorization validity may NOT be renewed.

Acute Promyelocytic Leukemia (APL)

- Induction/Consolidation Therapy:
  - Initial: Prior authorization validity will be provided initially for 6 months (180 days) [*1 cycle of induction therapy followed by consolidation therapy*].
  - Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter, based on response to therapy (*refer to Section V*).
- Therapy for first relapse:
  - Initial: Prior authorization validity will be provided initially for 6 months (180 days), unless otherwise specified.

        - ❖ Single-agent therapy: Prior authorization validity will be provided for 12 weeks (6 total doses).
    - Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter based on response to therapy (*refer to Section V*), unless otherwise specified.
        - ❖ Single-agent therapy: Prior authorization validity may NOT be renewed
- Therapy for leukocytosis associated with differentiation syndrome:
    - Initial: Prior authorization validity will be provided initially for 6 months (180 days) consisting of 1 cycle (up to 3 total doses).
    - Renewal: Prior authorization validity may NOT be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- AML:
    - Induction: 135 billable units on Day 1, 90 billable units on Day 4, 90 billable units on Day 7 of a 28-day cycle (1 cycle only)
    - Consolidation/Continuation: 225 billable units every 28 days
- APL:
    - Induction: 180 billable units on Day 1
    - Consolidation/Relapse: 270 billable units every 28 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years of age (unless otherwise specified); **AND**
- Member has not previously received gemtuzumab ozogamicin; **AND**
- Baseline electrocardiogram (ECG) has been obtained in members with a history of or predisposition for QTc prolongation; **AND**

Universal Criteria [1]

- Member has CD33-positive disease; **AND**

Acute Myeloid Leukemia (AML) † ‡ Φ [1,6,10]

- Member has newly-diagnosed disease; **AND**
    - Used in combination with daunorubicin and cytarabine **†**; **AND**
        - Member is at least 1 month of age; **OR**
    - Used as a single agent **†**; **OR**
    - Used in combination with cytarabine and idarubicin; **AND**
        - Used as induction or consolidation therapy; **AND**

        - Member has favorable or intermediate-risk AML; **OR**
    - Used in combination with high-dose cytarabine; **AND**
        - Used as consolidation therapy; **AND**
        - Member has favorable-risk AML; **OR**
- Member has relapsed or refractory disease; **AND**
    - Used as a single agent **†**; **AND**
    - Member is at least 2 years of age; **OR**
- Member has acute promyelocytic leukemia (APL); **AND**
    - Used for low-risk disease (white blood cell count ≤10 x 10^9/L); **AND**
        - Used as induction or consolidation therapy; **AND**
            - Used in combination with tretinoin (ATRA); **AND**
            - Arsenic is not available or is contraindicated; **OR**
    - Used for high-risk disease (white blood cell count >10 x 10^9/L); **AND**
        - Used as induction therapy; **AND**
            - Used in combination with tretinoin (ATRA) with or without arsenic trioxide (ATO); **OR**
        - Used as consolidation therapy; **AND**
            - Used in combination with tretinoin (ATRA) or arsenic trioxide (ATO); **OR**
    - Used for first relapse (morphologic or molecular); **AND**
        - Used as a single agent; **AND**
            - Used for early relapse (<6 months) after tretinoin (ATRA) and arsenic trioxide (ATO); **OR**
        - Used in combination with ATO (with or without ATRA); **AND**
            - Member has no prior exposure to ATO; **OR**
            - Used for early relapse (<6 months) after an ATRA + anthracycline-containing regimen; **OR**
            - Used for late relapse (≥ 6 months) after an ATO containing regimen; **OR**
    - Used for leukocytosis associated with differentiation syndrome; **AND**
        - Used as a single agent for difficult-to-treat cases

† FDA Approved Indication(s); **‡** Compendium Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria [1,6]

Prior authorization validity may be renewed based upon the following criteria:

- Member continues to meet the universal and indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded *(refer to Section I)*; **AND**

- Disease stabilization or improvement as evidenced by a complete response [CR] (i.e., morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion-related reactions (including anaphylaxis), hemorrhage, hepatotoxicity (e.g., veno-occlusive liver disease [VOD], sinusoidal obstruction syndrome [SOS], etc.), QT interval prolongation, etc.

V. Dosage/Administration [1,5-8,11]

Indication	Dose
Acute Myeloid Leukemia	**Newly Diagnosed AML**

	Adult (≥ 18 years old) – Combination regimen:
	• Induction Therapy (1 cycle only):
	  ○ Administer 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin or idarubicin and cytarabine
	  ○ For members requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle
	• Consolidation Therapy (maximum of 2 cycles):
	  ○ Administer 3 mg/m^2 (up to one 4.5 mg vial) on Day 1 in combination with daunorubicin or idarubicin and cytarabine
	  ○ Administer 3 mg/m^2 (up to one 4.5 mg vial) on Day 1 in combination with high-dose cytarabine
	Pediatric (1 month to < 18 years old) – Combination regimen:
	• Induction Therapy (1 cycle only):
	  ○ Administer 3 mg/m^2 (BSA ≥ 0.6 m^2) or 0.1 mg/kg (BSA < 0.6 m^2) on Day 6 in combination with daunorubicin and cytarabine
	  ○ For members requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle
	• Consolidation/Intensification Therapy (1 cycle only):
	  ○ Administer 3 mg/m^2 (BSA ≥ 0.6 m^2) or 0.1 mg/kg (BSA < 0.6 m^2) on Day 7 in intensification 2
	Adult (≥ 18 years old) – Single-agent regimen:
	• Induction Therapy (1 cycle only):
	  ○ Administer 6 mg/m^2 as a single agent on Day 1 and 3 mg/m^2 on Day 8
	• Continuation Therapy (maximum of 8 cycles):
	  ○ Administer 2 mg/m^2 as a single agent on Day 1 every 4 weeks; OR
	  ○ Administer 6 mg/m^2 as a single agent on Day 1 and 3 mg/m^2 on Day 8

	Relapsed or Refractory AML
	• Administer 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 (1 cycle only)
	Acute Promyelocytic Leukemia (APL)
	Low-Risk Disease: • Induction Therapy (1 cycle only): ○ Administer 6-9 mg/m^2 on Day 5 in combination with ATRA

	• Consolidation Therapy:
	  ○ Administer 6-9 mg/m^2 given monthly until achievement of complete molecular response.
	High-Risk Disease:
	• Induction Therapy (1 cycle only):
	  ○ Administer 6-9 mg/m^2 on Day 1 (or Day 2, Day 3, or Day 4) in combination with ATRA with or without ATO
	• Consolidation Therapy:
	  ○ ATRA and ATO are used for consolidation. If ATRA or ATO are discontinued due to toxicity, a single dose of gemtuzumab ozogamicin 6 or 9 mg/m^2 may be given once every 4-5 weeks provided platelets and ANC recover to ≥100 x 10^9/L and ≥1.0 x 10^9/L, respectively, until molecular complete remission.
	Therapy for First Relapse:
	• Single-agent:
	  ○ Administer 6 mg/m^2 on Day 1 and Day 15 (up to a maximum of 6 total doses)
	• In combination with ATO (with or without ATRA):
	  ○ Administer 9 mg/m^2 on Day 1 as a single dose until count recovery with marrow confirmation of remission.
	Therapy for leukocytosis associated with differentiation syndrome:
	• Administer 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 (1 cycle only)

VI. Billing Code/Availability Information

HCPCS Code:

- J9203 – Injection, gemtuzumab ozogamicin, 0.1 mg; 1 billable unit = 0.1 mg

NDC:

- Mylotarg 4.5 mg single-dose vial: 00008-4510-xx

VII. References

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C92.00	Acute myeloblastic leukemia not having achieved remission
C92.01	Acute myeloblastic leukemia in remission
C92.02	Acute myeloblastic leukemia in relapse
C92.40	Acute promyelocytic leukemia not having achieved remission
C92.41	Acute promyelocytic leukemia in remission
C92.42	Acute promyelocytic leukemia in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.51	Acute myelomonocytic leukemia in remission
C92.52	Acute myelomonocytic leukemia in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia in remission
C93.02	Acute monoblastic/monocytic leukemia in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC