Mylotarg™ (gemtuzumab ozogamicin)
(Intravenous)

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

Newly-Diagnosed AML

- In combination with daunorubicin and cytarabine (adult): Coverage will be provided for 6 months consisting of 3 cycles (1 induction and 2 consolidation) and may NOT be renewed.
- In combination with daunorubicin and cytarabine (pediatric): Coverage will be provided for 6 months consisting of 2 cycles (1 induction and 1 consolidation) and may NOT be renewed.
- Single-agent therapy: Coverage will be provided for 6 months and may be renewed. Coverage is provided for 1 cycle of induction and up to a maximum of 8 cycles of continuation.

Relapsed or Refractory AML

- Coverage will be provided for 6 months consisting of one cycle (3 doses) and may NOT be renewed.

Acute Promyelocytic Leukemia (APL)

- Induction/Consolidation Therapy: Coverage will be provided for 6 months and may be renewed. Coverage is provided for 1 cycle of induction therapy followed by consolidation therapy. *[Note: Duration of consolidation therapy is dependent on disease risk severity (see below)]*
    - Low-risk disease: Coverage will be provided until achievement of complete molecular response.
    - High-risk disease: Coverage will be provided until molecular complete response.
- Therapy for first relapse:
    - Single-agent therapy: Coverage will be provided for 6 total doses
    - Use in combination with arsenic trioxide: Coverage will be provided for 6 months and may be renewed until bone marrow confirmation of remission.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Mylotarg 4.5 mg single-dose vial: 7 vials per initial 28 days; 6 vials per 28 days thereafter

B. 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]

Coverage is provided in the following conditions:

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

Universal Criteria [1]

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

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

- Patient has newly-diagnosed disease; **AND**
  - Used in combination with daunorubicin and cytarabine †; **AND**
    - Patient is at least 1 month of age; **OR**
  - Used as a single agent †; **OR**
  - Used in combination with high-dose cytarabine; **AND**
    - Used as consolidation therapy in patients < 60 years of age; **AND**
    - Patient has NPM1-mutated and FLT3 negative favorable-risk AML; **OR**
- Patient has relapsed or refractory disease; **AND**
  - Used as a single agent †; **AND**
    - Patient is at least 2 years of age; **OR**
  - Used as a component of repeating the initial successful induction regimen if ≥12 months since induction regimen; **OR**
- Patient 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**
    - Patient 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

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

IV. Renewal Criteria [1,6]

Coverage may be renewed based upon the following criteria:

- Patient 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**
- 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.; **AND**
  - Patients receiving single-agent treatment for newly-diagnosed AML have not exceeded the maximum of 8 cycles of continuation (adult only); **OR**
  - Patients receiving consolidation therapy for acute promyelocytic leukemia (APL):

- Low-risk disease: Therapy will be discontinued once there is achievement of complete molecular response; **OR**
- High-risk disease: Therapy will be discontinued once there is achievement of molecular complete remission; **OR**

- Patients receiving therapy for first relapse of acute promyelocytic leukemia (APL):
  - Single-agent treatment: Coverage will be provided for 6 total doses
  - In combination with ATO (with or without ATRA): Therapy will be discontinued once there is bone marrow confirmation of remission

Note: treatment of newly diagnosed AML in combination with chemotherapy and relapsed or refractory AML may NOT be renewed.

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/m² (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine
	  ○ For patients requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle
	• Consolidation Therapy (maximum of 2 cycles):
	  ○ Administer 3 mg/m² (up to one 4.5 mg vial) on Day 1 in combination with daunorubicin and cytarabine *(may be given with high-dose cytarabine in patients < 60 years of age)*
	Pediatric (1 month to < 18 years old) – Combination regimen:
	• Induction Therapy (1 cycle only):
	  ○ Administer 3 mg/m² (BSA ≥ 0.6 m²) or 0.1 mg/kg (BSA < 0.6 m²) on Day 6 in combination with daunorubicin and cytarabine
	  ○ For patients requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle
	• Consolidation/Intensification Therapy (1 cycle only):
	  ○ Administer 3 mg/m² (BSA ≥ 0.6 m²) or 0.1 mg/kg (BSA < 0.6 m²) on Day 7 in intensification 2
	Adult (≥ 18 years old) – Single-agent regimen:
	• Induction Therapy (1 cycle only):
	  ○ Administer 6 mg/m² as a single agent on Day 1 and 3 mg/m² on Day 8
	• Continuation Therapy:
	  ○ Administer 2 mg/m² as a single agent on Day 1 every 4 weeks (maximum of 8 cycles); OR
	  ○ Administer 6 mg/m² as a single agent on Day 1 and 3 mg/m² on Day 8

	Relapsed or Refractory AML
	• Administer 3 mg/m² (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 9 mg/m² on Day 5 in combination with ATRA
	• Consolidation Therapy:
	  ○ Administer 9 mg/m² given monthly until achievement of complete molecular response.
	High-Risk Disease:
	• Induction Therapy (1 cycle only):
	  ○ Administer 6-9 mg/m² on Day 1 (or Day 2, Day 3, or Day 4) in combination with ATRA + 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 9mg/m² may be given once every 4-5 weeks provided platelets and ANC recover to ≥100 and ≥1.0, respectively, until molecular complete remission.
	Therapy for First Relapse:
	• Single-agent:
	  ○ Administer 6 mg/m² on Day 1 and Day 16 (up to a maximum of 6 total doses)
	• In combination with ATO (with or without ATRA):
	  ○ Administer 6-9 mg/m² on Day 1 as a single dose until count recovery with marrow confirmation of remission.

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

1. Mylotarg [package insert]. Philadelphia, PA; Pfizer Inc.; August 2021. Accessed October 2023.
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10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) gemtuzumab ozogamicin. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2023.
11. Estey EH, Giles FJ, Beran M, et al. Experience with gemtuzumab ozogamycin ("mylotarg") and all-trans retinoic acid in untreated acute promyelocytic leukemia. Blood. 2002 Jun 1;99(11):4222-4. doi: 10.1182/blood-2001-12-0174. PMID: 12010830.
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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)

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp
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
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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