Mylotarg™ (gemtuzumab ozogamicin)
(Intravenous)

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I. Length of Authorization

Newly-Diagnosed AML

- De novo disease 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.
- De novo disease 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 use: 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.

Post-Induction Therapy for AML

- Coverage will be provided for 6 months consisting of 2 cycles (2 doses) and may not be renewed.

Consolidation Therapy for AML

- Coverage will be provided for 6 months consisting of 2 cycles (2 doses) and may not be renewed.

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

- 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 28 weeks from complete response.

- Therapy after first relapse: 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: 5 vials per initial 28 days; 1 vial per 28 days thereafter

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

	Induction (1 cycle only)	Consolidation
AML	135 billable units on Day 1 & 90 billable units on Day 8 of a 28-day cycle	45 billable units on Day 1 of a 28-day cycle (up to a maximum of 8 subsequent cycles)
APL	180 billable units on Day 1	180 billable units on Day 1 of a 28-day cycle

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) 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 has de novo disease †; **AND**
      - Patient is at least 1 month of age; **OR**
    - Patient has favorable-risk cytogenetics or intermediate-risk disease; **OR**
  - Used as a single agent †; **OR**
- Used as post-induction therapy; **AND**
  - Used in combination with daunorubicin and intermediate-dose cytarabine; **AND**
  - Patient is ≥ 60 years of age and obtained a complete response to previous intensive therapy; **AND**
  - Patient is able to receive conventional consolidation therapy; **OR**
- Used as consolidation therapy; **AND**
  - Patient is < 60 years of age; **AND**
    - Used in combination with high-dose cytarabine for NPM1 positive and FLT3 negative disease; **AND**

        - Patient has core binding factor (CBF) cytogenetic translocations and minimal residual disease (MRD) negative; **OR**
    - Used in combination with daunorubicin and intermediate-dose cytarabine; **AND**
        - Patient has core binding factor (CBF) cytogenetic translocations and minimal residual disease (MRD) negative; **OR**
        - Patient has intermediate-risk cytogenetics and/or molecular abnormalities, including MRD positive; **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 late relapse (≥12 months since induction regimen); **OR**
- Patient has acute promyelocytic leukemia (APL) ‡; **AND**
    - Used as induction or consolidation therapy in patients with low-risk disease (white blood cell count ≤10 X 10^9/L); **AND**
        - Used in combination with tretinoin (ATRA); **AND**
        - Arsenic is not available or is contraindicated; **OR**
    - Used as induction or consolidation therapy in patients with high risk disease (white blood cell count >10 X 10^9/L); **AND**
        - Used in combination with tretinoin (ATRA) and/or arsenic trioxide (ATO); **OR**
    - Used for first relapse (morphologic or molecular) in combination with arsenic trioxide (ATO); **AND**
        - Used for late relapse (≥ 6 months) after an arsenic trioxide (ATO) containing regimen; **OR**
        - Used for early relapse (<6 months) after tretinoin (ATRA) + anthracycline-containing regimen; **OR**
        - Patient is arsenic trioxide (ATO)-naïve

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

IV. Renewal Criteria [1,6]

Coverage can 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 including hepatic veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS), 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 after 28 weeks from achievement of complete response; **OR**
    - Patients receiving therapy for first relapse of acute promyelocytic leukemia (APL):
        - Therapy will be discontinued once there is bone marrow confirmation of remission

Note: treatment of newly diagnosed de novo AML, relapsed or refractory AML, post-induction therapy for AML, and consolidation therapy for AML are not renewable.

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

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

	Adult (≥ 18 years old) – Combination regimen (De Novo AML):
	• Induction Therapy (1 cycle only):
	  ○ 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):
	  ○ 3 mg/m² (up to one 4.5 mg vial) on Day 1 in combination with daunorubicin and cytarabine
	Pediatric (1 month to < 18 years old) – Combination regimen (De Novo AML):
	• Induction Therapy (1 cycle only):
	  ○ 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):
	  ○ 3 mg/m² (BSA ≥ 0.6 m²) or 0.1 mg/kg (BSA < 0.6 m²) on Day 7 in Intensification 2
	Single-agent regimen:
	• Induction Therapy (1 cycle only):
	  ○ 6 mg/m² as a single agent on Day 1, and 3 mg/m² on Day 8
	• Continuation Therapy (maximum of 8 cycles):
	  ○ 2 mg/m² as a single agent on Day 1 every 4 weeks

	Post-Induction Therapy for AML

	≥ 60 years of age – Combination regimen: • 3 mg/m² (up to one 4.5 mg vial) on day 1 in combination with daunorubicin and intermediate-dose cytarabine (2 cycles only)
	Consolidation Therapy for AML
	< 60 years of age – Combination regimen: • 3 mg/m² (up to one 4.5 mg vial) on day 1 in combination with daunorubicin and intermediate-dose cytarabine (2 cycles only) • 3 mg/m² (up to one 4.5 mg vial) on day 1 in combination with high-dose cytarabine (2 cycles only)
	Relapsed or Refractory AML (single agent)
	• 3 mg/m² (up to one 4.5 mg vial) on Days 1, 4, and 7 (1 cycle only)
	Acute Promyelocytic Leukemia

	Combination regimen:
	• Induction Therapy for **low-risk** disease (1 cycle only):
	  ○ 9 mg/m² on Day 5 in combination with ATRA
	• Induction Therapy for **high-risk** disease (1 cycle only):
	  ○ 6-9 mg/m² on Day 1 (or Day 2 or Day 3 or Day 4) in combination with ATRA+ATO
	• Consolidation Therapy for **low-risk** disease:
	  ○ 9 mg/m² given monthly until achievement of complete molecular response.
	• Consolidation Therapy for **high-risk** disease:
	  ○ ATRA and ATO are used for consolidation. If ATRA or ATO are discontinued due to toxicity then: Mylotarg, single agent, dosed at 9mg/m² once every 4-5 weeks until 28 weeks from complete remission.
	• Therapy for First Relapse
	  ○ 6-9 mg/m² on Day 1 in combination with ATO 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 September 2022.
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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 2.2022. National Comprehensive Cancer Network, 2022. 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 September 2022.
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9. Gamis AS, Alonzo TA, Meshinchi S, et al. Gemtuzumab ozogamicin in children and adolescents with de novo acute myeloid leukemia improves event-free survival by reducing relapse risk: results from the randomized phase III Children's Oncology Group trial AAML0531. J Clin Oncol. 2014;32(27):3021-3032. doi:10.1200/JCO.2014.55.3628.
10. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) gemtuzumab ozogamicin. National Comprehensive Cancer Network, 2022. 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 September 2022.
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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)

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