Mylotarg™ (gemtuzumab ozogamicin)
(Intravenous)

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Document Number: IC-0491

Date Approved: 12/03/2024
Date of Origin: 09/03/2019
Dates Reviewed: 09/2019, 12/2019, 11/2020, 12/2021, 12/2022, 12/2023, 11/2024

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.
- In combination with high-dose cytarabine (adult) as consolidation therapy: Coverage will be provided for 6 months consisting of 2 cycles (2 doses) 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 1 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)]*
    - High-risk disease: Coverage for consolidation therapy will be provided for 2 cycles.
- 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.
- Therapy for leukocytosis associated with differentiation syndrome:
    - Coverage will be provided for one cycle (up to 3 total doses) and 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: 270 billable units every 28 days (2 cycles only)

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; **AND**
    - Patient has 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**
- Patient has acute promyelocytic leukemia (APL); **AND**
  - 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) and arsenic trioxide (ATO); **OR**
    - Used as consolidation therapy; **AND**
      - Used following treatment with tretinoin (ATRA) and arsenic trioxide (ATO); **OR**
  - Used for first relapse **Ω** (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; **OR**
- Used for leukocytosis associated with differentiation syndrome **Ω**; **AND**
    - Used as a single agent for difficult-to-treat cases

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

Ω *Please note that the supporting data for this indication has been assessed and deemed to be of insufficient quality based on the review conducted for the Enhanced Oncology Value (EOV) program. However, due to the absence of viable alternative treatment options, this indication will be retained in our policy and evaluated on a case-by-case basis.*

† 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.), QTc 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):
        - High-risk disease: Therapy has not exceeded the maximum of 2 cycles; **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; **OR**

- Patients receiving therapy for leukocytosis associated with differentiation syndrome:
  - Coverage may NOT be renewed

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

V. Dosage/Administration [1,5-8,11,13,14]

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 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/m^2 (up to one 4.5 mg vial) on Day 1 in combination with daunorubicin 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 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/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:
	  ○ Administer 2 mg/m^2 as a single agent on Day 1 every 4 weeks (maximum of 8 cycles); 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)
	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 + ATO • Consolidation Therapy: ○ Administer 9 mg/m^2 for 2 cycles 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 of 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 (STANDARD)

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VIII. References (ENHANCED)

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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)

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