Mylotarg (gemtuzumab ozogamicin)
(Intravenous)

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I. Length of Authorization

Newly-Diagnosed AML

- De novo disease in combination with daunorubicin and cytarabine: coverage will be provided for 6 months consisting of 3 cycles (1 induction and 2 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.

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

- 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 7 cycles of consolidation/continuation.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Mylotarg 4.5 mg vial: 5 vials per initial 28 days; 1 vial per 28 days thereafter (up to a maximum of 8 cycles)

B. Max Units (per dose and over time) [Medical Benefit]:

	Induction (1 cycle only)	Consolidation
AML	▾ 135 billable units on Day 1 & 90 billable units on Day 8 of a 28-day cycle; OR ▾ 45 billable units on Days 1, 4, & 7 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 (up to a maximum of 7 subsequent cycles)

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient has CD33-positive disease; AND
- Patients with a history of or predisposition for QTc prolongation have a baseline electrocardiogram (ECG); AND
- Patients with hyperleukocytosis (leukocyte count ≥ 30 x 10^9/L) have had cytoreduction; AND
- Patient has not previously received gemtuzumab ozogamicin; AND

Acute Myeloid Leukemia (AML) †

- Patient has newly-diagnosed disease; AND
  - Patient is 18 years or older; AND
    - Used in combination with daunorubicin and cytarabine; AND
      - Patient has de novo disease; AND
      - Patient does not have adverse-risk cytogenetics OR cytogenetic results are not yet known; OR
    - Used as a single agent; OR
- Used as post-remission therapy in patient who obtained a complete or partial response to previous treatment for AML; AND
  - Used in combination with daunorubicin and cytarabine; AND
    - Patient obtained a complete response to previous therapy; OR
    - Patient does not have adverse-risk cytogenetics OR cytogenetic results are not yet known; OR
  - Used as a single agent in patients with a response to previous therapy; OR
- Patient has relapsed or refractory disease; AND
  - Patient is 2 years or older; AND
    - Must be used as a single agent; OR
    - Used as part of re-induction therapy if relapse is occurring at least 12 months after successful initial response; OR
- Patient has acute promyelocytic leukemia ‡; AND
  - Used as induction and 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; AND
    - Used for a late relapse after at least 6 months of initial response after an ATO containing regimen; OR
    - Used for an early relapse with an initial response from tretinoin and anthracycline regimen of less than 6 months in ATO-naïve patients

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s)

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria 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 the following: severe infusion-related reactions, hemorrhage, hepatotoxicity including hepatic veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS), tumor lysis syndrome, symptomatic QTc prolongation, etc.; AND
    - Patients with newly-diagnosed AML have not exceeded the maximum of 8 cycles of continuation; OR
    - Patients with acute promyelocytic leukemia (APL) have not exceeded the maximum of 7 cycles of therapy

Note: treatment of newly diagnosed de novo AML as well as relapsed or refractory AML are not renewable

V. Dosage/Administration

Indication	Dose
Acute Myeloid Leukemia	Newly Diagnosed AML

	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
	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

	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 (1 cycle only):

	○ 6-9 mg/m² on Day 1 in combination with ATRA+ATO • Consolidation Therapy (up to a maximum of 7 cycles): ○ ATRA and ATO are used for consolidation. If ATRA or ATO are discontinued due to toxicity then: Mylotarg, single agent, dosed at 9mg/m2 on Day 1 every 4-5 weeks until 28 weeks from complete remission

- Refrigerate (2-8°C; 36-46°F) and store in the original carton to protect from light. Do not freeze.
- Note: cycle lengths are 28 days

VI. Billing Code/Availability Information

Jcode:

- J9203 – Injection, gemtuzumab ozogamicin, 0.1 mg: 1 billable unit = 0.1 mg (Effective 1/1/2018)

NDC:

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

VII. References

1. Mylotarg [package insert]. Philadelphia, PA; Pfizer Inc., April 2018. Accessed October 2018.
2. Castaigne S, Pautas C, Terré C, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012 Apr 21;379(9825):1508-16
3. Amadori S, Suciu S, Selleslag D, et al. Gemtuzumab Ozogamicin Versus Best Supportive Care in Older Patients With Newly Diagnosed Acute Myeloid Leukemia Unsuitable for Intensive Chemotherapy: Results of the Randomized Phase III EORTC-GIMEMA AML-19 Trial. J Clin Oncol. 2016 Mar 20;34(9):972-9.
4. Taksin AL, Legrand O, Raffoux E, et al. High efficacy and safety profile of fractionated doses of Mylotarg as induction therapy in patients with relapsed acute myeloblastic leukemia: A prospective study of the ALFA group. Leukemia 2007;21:66–71.
5. Abaza Y, Kantarjian H, Garcia-Mannero G, et al. Long-term outcome of acute promyelocytic leukemia treated with all-transretinoic acid, arsenic trioxide, and gemtuzumab. Blood 2017;129:1275-1283.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Myeloid Leukemia. Version 3.2017. National Comprehensive Cancer Network, 2018. 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 2017.

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
C94.00	Acute erythroid leukemia not having achieved remission
C94.01	Acute erythroid leukemia in remission
C94.02	Acute erythroid leukemia in relapse
C94.20	Acute megakaryoblastic leukemia not having achieved remission
C94.21	Acute megakaryoblastic leukemia in remission
C94.22	Acute megakaryoblastic 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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-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): 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

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