

## 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.

#### Post-Remission 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

- 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) [NDC Unit]:

- 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) [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; <b>OR</b>	• 45 billable units on Day 1 of a 28-day cycle (up to a maximum of 8 subsequent cycles)

	•45 billable units on Days 1, 4, & 7 of a 28-day cycle	
<b>APL</b>	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  $\geq 30 \times 10^9/L$ ) have had cytoreduction; **AND**
- Patient has not previously received gemtuzumab ozogamicin; **AND**
- Patient is 18 years or older (unless otherwise specified); **AND**

#### Acute Myeloid Leukemia (AML) †

- Patient has newly-diagnosed disease; **AND**
  - Used in combination with daunorubicin and cytarabine; **AND**
    - Patient has de novo disease †; **AND**
    - Patient has favorable or intermediate-risk cytogenetics; **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 is at least 60 years old and obtained a complete response to previous therapy; **OR**
    - Patient is less than 60 years old with core binding factor (CBF) cytogenetic translocations without KIT mutations or intermediate-risk cytogenetics and/or molecular abnormalities; **OR**
  - Used in combination with high-dose cytarabine; **AND**
    - Patient is less than 60 years old with core binding factor (CBF) cytogenetic translocations without KIT mutations; **OR**
- Patient has relapsed or refractory disease; **AND**
  - Patient is 2 years or older; **AND**
  - Must be used as a single agent †; **OR**
- Patient has acute promyelocytic leukemia ‡; **AND**
  - Used as induction and consolidation therapy in patients with high risk disease (white blood cell count  $>10 \times 10^9/L$ ); **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 a late relapse ( $\geq 6$  months) of initial response after an arsenic trioxide (ATO) containing regimen; **OR**
- Used for an 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)

#### 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 cytogenetic 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, relapsed or refractory AML, and post-remission therapy for AML are not renewable.

#### V. Dosage/Administration

Indication	Dose
Acute Myeloid Leukemia	<p><b>Newly Diagnosed AML</b></p> <p><u>Combination regimen (De Novo AML):</u></p> <ul style="list-style-type: none"> <li>• Induction Therapy (1 cycle only): <ul style="list-style-type: none"> <li>○ 3 mg/m<sup>2</sup> (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine</li> <li>○ For patients requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle</li> </ul> </li> <li>• Consolidation Therapy (maximum of 2 cycles): <ul style="list-style-type: none"> <li>○ 3 mg/m<sup>2</sup> (up to one 4.5 mg vial) on Day 1 in combination with daunorubicin and cytarabine</li> </ul> </li> </ul> <p><u>Single-agent regimen:</u></p> <ul style="list-style-type: none"> <li>• Induction Therapy (1 cycle only):</li> </ul>

<ul style="list-style-type: none"> <li>○ 6 mg/m<sup>2</sup> as a single agent on Day 1, and 3 mg/m<sup>2</sup> on Day 8</li> <li>• Continuation Therapy (maximum of 8 cycles): <ul style="list-style-type: none"> <li>○ 2 mg/m<sup>2</sup> as a single agent on Day 1 every 4 weeks</li> </ul> </li> </ul>
<b>Post-Remission Therapy for AML</b>
<u>Combination regimen:</u> <ul style="list-style-type: none"> <li>• 3 mg/m<sup>2</sup> (up to one 4.5 mg vial) on day 1 in combination with daunorubicin and cytarabine (2 cycles only)</li> <li>• 3 mg/m<sup>2</sup> (up to one 4.5 mg vial) on day 1 in combination with high-dose cytarabine (2 cycles only)</li> </ul>
<b>Relapsed or Refractory AML (single agent)</b>
<ul style="list-style-type: none"> <li>• 3 mg/m<sup>2</sup> (up to one 4.5 mg vial) on Days 1, 4, and 7 (1 cycle only)</li> </ul>
<b>Acute Promyelocytic Leukemia</b>
<u>Combination regimen:</u> <ul style="list-style-type: none"> <li>• Induction Therapy (1 cycle only): <ul style="list-style-type: none"> <li>○ 6-9 mg/m<sup>2</sup> on Day 1 in combination with ATRA+ATO</li> </ul> </li> <li>• Consolidation Therapy (up to a maximum of 7 cycles): <ul style="list-style-type: none"> <li>○ ATRA and ATO are used for consolidation. If ATRA or ATO are discontinued due to toxicity then: Mylotarg, single agent, dosed at 9mg/m<sup>2</sup> on Day 1 every 4-5 weeks until 28 weeks from complete remission</li> </ul> </li> </ul>

- 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

### 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., April 2018. Accessed November 2019.
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, Suci 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, 2019. 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 November 2019.
7. Burnett AK, Hills RK, Milligan D, et al. Identification of patients with acute myeloblastic leukemia who benefit from the addition of gemtuzumab ozogamicin: results of the MRC AML15 trial. *J Clin Oncol.* 2011 Feb 1;29(4):369-77. doi: 10.1200/JCO.2010.31.4310. Epub 2010 Dec 20.
8. Hills RK, Castaigne S, Appelbaum FR, et al. Addition of gemtuzumab ozogamicin to induction chemotherapy in adult patients with acute myeloid leukaemia: a meta-analysis of individual patient data from randomised controlled trials. *Lancet Oncol.* 2014 Aug;15(9):986-96. doi: 10.1016/S1470-2045(14)70281-5. Epub 2014 Jul 6.
9. CGS, Administrators, LLC. Local Coverage Article (LCA): Billing and Coding: Gemtuzumab Ozogamicin; Mylotarg -J9203 (A57249). Centers for Medicare & Medicaid Services, Inc. Updated on 09/18/2019 with effective date 09/26/2019. Accessed November 2019.
10. Palmetto GBA, LLC. Local Coverage Article (LCA): Billing and Coding: Chemotherapy (A56141). Centers for Medicare & Medicaid Services, Inc. Updated on 10/21/2019 with effective date 10/31/2019. Accessed November 2019.

## 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), Local Coverage Determinations (LCDs), and Articles 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/Article):

<b>Jurisdiction(s):</b> 15	<b>NCD/LCD/Article Document (s):</b> A57249
<a href="https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57249&amp;ver=2&amp;DocID=A57249&amp;bc=gAAAAABAAAA&amp;">https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57249&amp;ver=2&amp;DocID=A57249&amp;bc=gAAAAABAAAA&amp;</a>	

<b>Jurisdiction(s):</b> J & M	<b>NCD/LCD/Article Document (s):</b> A56141
<a href="https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57249&amp;ver=2&amp;DocID=A56141&amp;bc=gAAAAABAAAA&amp;">https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=57249&amp;ver=2&amp;DocID=A56141&amp;bc=gAAAAABAAAA&amp;</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.

<b>Medicare Part B Administrative Contractor (MAC) Jurisdictions</b>		
<b>Jurisdiction</b>	<b>Applicable State/US Territory</b>	<b>Contractor</b>
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