Approved Revision: Do Not Implement Until 4/2/21

Gemtuzumab Ozogamicin

NDC CODE(S) 00008-4510-xx MYLOTARG 4.5MG Solution Reconstituted (PFIZER U.S.)

DESCRIPTION

Gemtuzumab ozogamicin is a CD33-directed antibody-drug conjugate (ADC). The antibody portion (hP67.6) recognizes human CD33 antigen. The small molecule, N-acetyl gamma calicheamicin, is a cytotoxic agent that is covalently attached to the antibody via a linker. Nonclinical data suggest that the anticancer activity of gemtuzumab ozogamicin is due to the binding of the ADC to CD33-expressing tumor cells, followed by internalization of the ADC-CD33 complex, and the intracellular release of N-acetyl gamma calicheamicin dimethyl hydrazide via hydrolytic cleavage of the linker. Activation of N-acetyl gamma calicheamicin dimethyl hydrazide induces double-strand DNA breaks, subsequently inducing cell cycle arrest and apoptotic cell death.

POLICY

- Gemtuzumab ozogamicin for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Acute myeloid leukemia (AML)
  - Acute Promyelocytic Leukemia (PML) (subtype of AML)
- Gemtuzumab ozogamicin for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Gemtuzumab ozogamicin is considered **medically appropriate** if **ALL** of the following criteria are met:
  - The individual has CD33-positive disease
  - Individual with a history of or predisposition for QTc prolongation has a baseline electrocardiogram (ECG)
  - The individual has not previously received gemtuzumab ozogamicin
  - Individual is 18 years of age or older unless otherwise specified
  - Diagnosis of **ANY ONE** of the following:
    - Acute Myeloid Leukemia (AML) if **ANY ONE** of the following:
      - Disease is newly diagnosed and used as **ANY ONE** of the following:
        - In combination with daunorubicin and cytarabine if **ALL** of the following
          - Individual has de novo disease and is one month of age or older
          - Individual has favorable or intermediate-risk cytogenetics
        - Used as a single agent
      - Used as post-remission therapy if **ANY ONE** of the following:
        - Used in combination with daunorubicin and intermediate-dose cytarabine if **ANY ONE** of the following:
          - Individual 60 years of age or older with complete response to previous intensive therapy
          - Individual less than 60 years of age with core binding factor (CBF) cytogenetic translocations without KIT mutations or intermediate-risk cytogenetics and/or molecular abnormalities
        - Used in combination with high-dose cytarabine in individual less than or equal to 60 years of age with core binding factor (CBF) cytogenetic translocations without KIT mutations
      - Disease is relapsed or refractory if **ANY ONE** of the following:
        - Used as a single agent if individual is 2 years of age or older
        - Used as a component of the repetition of the initial successful induction regimen if late relapse (≥12 months since induction regimen)

- Acute Promyelocytic Leukemia if used as **ANY ONE** of the following:
  - Induction and consolidation therapy for high risk disease (i.e., white blood cell count >10 X 10^9/L) in combination with tretinoin (ATRA) and/or arsenic trioxide (ATO)
  - First relapse (morphologic or molecular) in combination with arsenic trioxide for **ANY ONE** of the following:
    - Late relapse (>6 months) of initial response after an arsenic trioxide (ATO)-containing regimen
    - Early relapse (<6 months) after tretinoin (ATRA) and anthracycline-containing regimen
    - Individual is arsenic trioxide (ATO)-naive

RENEWAL CRITERIA

- Gemtuzumab ozogamicin is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria not including prerequisite therapy
  - Tumor response with stabilization of disease or decrease in size of tumor or tumor spread
  - Disease stabilization or improvement as evidenced by a complete response (CR), e.g., morphologic, cytogenetic or molecular complete response, complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH
  - Absence of unacceptable toxicity from the drug, e.g., severe infusion-related reactions, hemorrhage, hepatotoxicity including hepatic veno-occlusive disease (VOD)/sinusoidal obstruction syndrome (SOS), QT~~c~~ interval prolongation, etc.,
  - Individual receiving **ANY ONE** of the following:
    - Single-agent treatment for newly-diagnosed AML (adult only) has not exceeded the maximum of 8 cycles of continuation
    - Consolidation therapy for Acute Promyelocytic Leukemia (APL) has not exceeded the maximum of 7 cycles of therapy
    - Therapy for first relapse of Acute Promyelocytic leukemia (APL) – individual will discontinue therapy once there is bone marrow confirmation of remission

Note: Treatment of newly diagnosed de novo AML, relapsed or refractory AML and post-remission therapy for AML is not renewable

INDICATION(S)	DOSAGE & ADMINISTRATION
Acute Myeloid Leukemia	**De Novo AML - Adult (18 years of age or older) - Combination regimen:** 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 individual 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 **De Novo AML - Pediatric (1 month of age to < 18 years) - Combination regimen:** 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 individual requiring a second induction cycle, do not administer gemtuzumab ozogamicin during the second induction cycle Consolidation/Intensification Therapy (1 cycle only): • o 3 mg/m2 (BSA ≥ 0.6 m2) or 0.1 mg/kg (BSA < 0.6 m2) on Day 7 in • Intensification 2

	De Novo AML - 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-Remission Therapy for AML** Combination regimen: • 3 mg/m2 (up to one 4.5 mg vial) on day 1 in combination with daunorubicin and 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 (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 Therapy for first relapse: • 6-9 mg/m2 on Day 1 in combination with ATO until count recovery with marrow confirmation of remission

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 consolidations) and may not be renewed.
  - 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-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
- Induction/Consolidation 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 7 cycles of consolidation/continuation.
- Therapy after first relapse: Coverage will be provided for 6 months and may be renewed until bone marrow confirmation of remission.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Lexicomp Online. (2020). AHFS DI. *Fluocinolone.* Retrieved July 29, 2020 from Lexicomp Online with AHFS.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, June). *Gemtuzumab ozogamicin*. Retrieved July 29, 2020 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. *Gemtuzumab ozogamicin.* Retrieved November 30, 2020 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2020, June). Center for Drug Evaluation and Research. MYLOTARG™ (gemtuzumab ozogamicin). Retrieved July 29, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761060s004lbl.pdf.

EFFECTIVE DATE 4/2/21

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