VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION REVIEW MEDICAL POLICY

POLICY: Oncology (Injectable) – Mylotarg Utilization Review Medical Policy
- Mylotarg™ (gemtuzumab ozogamicin for injection – Pfizer)

REVIEW DATE: 07/15/2020

Overview
Mylotarg, an antibody-drug conjugate directed towards the CD33 antigen, is indicated for the treatment of:
- **CD33-positive acute myeloid leukemia (AML)**, newly diagnosed, in adults and pediatric patients ≥ 1 month of age; AND
- **CD33-positive AML**, relapsed or refractory, in adults and pediatric patients 2 years and older.[1]

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for AML (version 3.2020 – December 23, 2019) recommend Mylotarg for induction therapy, post-remission therapy, and for relapsed/refractory CD33-positive AML.[2,3] Mylotarg can be used as a single agent or in combination with cytarabine and daunorubicin. The NCCN guidelines for AML also recommend Mylotarg for induction and consolidation therapy in patients ≥ 18 years of age with high-risk (white blood cell count > 10,000/µL) acute promyelocytic leukemia, and for relapsed disease. Mylotarg can be used in combination with tretinoin and/or arsenic trioxide.

Acute Promyelocytic Leukemia – Dosing in First Morphologic or Molecular Relapse
In a pilot study, the safety and efficacy of Mylotarg in patients with acute promyelocytic leukemia in molecular relapse (N = 16) was assessed.[4] In this study, patients received up to 6 doses of Mylotarg 6 mg/m^2. Fourteen of 16 patients achieved molecular remission, seven patients achieved a sustained response lasting for a median of 15 months and seven patients relapsed between 3 and 15 months.

In a second pilot study, eight acute promyelocytic leukemia patients in first relapse were treated with arsenic trioxide, all-trans retinoic acid and Mylotarg.[5] Patients received Mylotarg 9 mg/m^2 IV given once monthly for 10 months. After consolidation, patients received maintenance therapy which included idarubicin, all-trans retinoic acid, 6-mercaptopurine and methotrexate. Three patients completed consolidation, the other five patients received between two and seven cycles of consolidation. All patients achieved complete response, after a median of 36 months of follow-up, six patients were alive in complete response and two died while in complete response.

Policy Statement
Prior authorization is recommended for medical benefit coverage of Mylotarg. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In the case where approval is authorized in months, 1 month is equal to 30 days.

Due to the specialized skills required for evaluation and diagnosis of patients treated with Mylotarg, as well as the monitoring required for adverse events and long-term efficacy, approval requires Mylotarg to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Mylotarg is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Acute Myeloid Leukemia – Newly Diagnosed CD33-Positive. Approve for 1 year if the patient meets the following criteria (A and B):
- **A)** Patient is ≥ 1 month of age; AND
- **B)** Mylotarg is prescribed by or in consultation with an oncologist.

Dosing. Approve one of the following dosing regimens (A or B):
- **A)** Adult patients ≥ 18 years of age (i, ii, and iii):
  - **i.** Each individual dose must not exceed 6 mg/m^2 administered intravenously; AND
  - **ii.** Administer up to 3 doses of Mylotarg during the initial (induction) cycle; AND
  - **iii.** Administer 1 dose of Mylotarg during each subsequent (consolidation) cycle.
- **B)** Pediatric patients 1 month to < 18 years of age (i, ii, and iii):
  - **i.** Patient meets ONE of the following (a or b):
    - **a)** Each individual dose must not exceed 3 mg/m^2 administered intravenously for patients with body surface area ≥ 0.6 m^2; OR
    - **b)** Each individual dose must not exceed 0.1 mg/kg for patients with body surface area < 0.6 m^2; AND
  - **ii.** Administer 1 dose of Mylotarg during the initial (induction) cycle; AND
  - **iii.** Administer 1 dose during the intensification phase.

2. Acute Myeloid Leukemia – Relapsed or Refractory CD33-Positive. Approve for 1 month if the patient meets the following criteria (A and B):
- **A)** Patient is ≥ 2 years of age; AND
- **B)** Mylotarg is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):
- **A)** Each individual dose must not exceed 4.5 mg administered intravenously; AND
- **B)** Administer no more than 3 doses of Mylotarg.

Other Uses with Supportive Evidence

3. Acute Promyelocytic Leukemia – High-Risk. Approve for 6 months if the patient meets the following criteria (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has high risk disease, defined as a white blood cell count > 10,000/mcL; AND
- **C)** Mylotarg is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):
- **A)** Each individual dose of Mylotarg must not exceed 9 mg/m^2 administered intravenously; AND
- **B)** Mylotarg is administered no more frequently than once every 28 days.[2]

4. Acute Promyelocytic Leukemia – First Relapse (Morphologic or Molecular). Approve for 6 months if the patient meets the following criteria (A and B):
A) Patient is ≥ 2 years of age; AND
B) Mylotarg is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen (A and B):
A) Each individual dose of Mylotarg must not exceed 9 mg/m^2 administered intravenously; AND
B) Mylotarg is administered no more frequently than once every 28 days.[4-7]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Mylotarg is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Mylotarg™ for intravenous infusion [prescribing information]. Philadelphia, PA: Pfizer; June 2020.
2. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 3.2020 – December 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 7, 2020.
3. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 7, 2020. Search term: gemtuzumab.
4. Lo-Coco F, Cimino G, Breccia M, et al. Gemtuzumab Ozogamicin (Mylotarg) as a Single Agent for Molecularly Relapsed Acute Promyelocytic Leukemia. *Blood*. 2004;104:1995-1999.
5. Aribi A, Kantarjian HM, Estey EH, et al. Combination Therapy with Arsenic Trioxide, All-*trans* Retinoic Acid, and Gemtuzumab Ozogamicin in Recurrent Acute Promyelocytic Leukemia. *Cancer*. 2007;109:1355-1359.
6. Schwarz J, Markova J, Pekova S, et al. A Single Administration of Gemtuzumab Ozogamicin for Molecular Relapse of Acute Promyelocytic Leukemia. *Hematol J*. 2004;5:279-280.
7. Tsimberidou AM, Estey E, Whitman GJ, et al. Extramedullary Relapse in a Patient with Acute Promyelocytic Leukemia: Successful Treatment with Arsenic Trioxide, all-*trans* Retinoic Acid and Gemtuzumab Ozogamicin Therapies. *Leuk Res*. 2004;28:991-994.

History

Type of Revision	Summary of Changes	Review Date
New Policy	--	08/08/2018
Annual review	Revised approval duration for AML – Newly Diagnosed CD33-Positive to 1 year. Revised initial approval duration to 6 months for APL – High Risk. Removed Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics sections from each indication. Removed Waste Management and Other Cancer Indication sections.	07/17/2019
Annual review	**Acute Myeloid Leukemia – Newly Diagnosed CD33-Positive**. Revised approval criteria down to ≥ 1 month of age. Consolidated adult combination therapy and single agent therapy dosing regimens. Added dosing regimen for pediatric patients 1 month to < 18 years of age.	07/15/2020