Gemtuzumab ozogamicin (MYLOTARG)
Criteria for Use
November 2018

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at the *PBM INTERnet* or *PBM INTRAnet* site for further information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive gemtuzumab.

- ☐ Hypersensitivity to gemtuzumab or any of its components
- ☐ Pregnancy (known pregnancy or positive pregnancy test) and/or actively breastfeeding
- ☐ Tbili > 2x ULN, AST > 2.5x ULN, and ALT > 2.5x ULN
- ☐ Hyperleukocytosis defined as leukocyte count $\geq$ 30 Gi/L (see Issues for Consideration)
- ☐ Adverse-risk cytogenetics (see Issues for Consideration)

Inclusion Criteria

The answers to one of the following must be fulfilled in order to meet criteria:

- ☐ Previously untreated CD-33 positive acute myeloid leukemia (AML) in adults fit for intensive induction
  In combination with standard 7+3 induction of daunorubicin and cytarabine
- ☐ Previously untreated CD-33 positive acute myeloid leukemia (AML) in adults age $\geq$ 60 years
  As monotherapy, if patient is not a candidate for, or declines intensive induction
- ☐ Relapsed or refractory CD-33 positive AML in adults, as monotherapy

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For women of childbearing potential

- ☐ Pregnancy should be excluded prior to receiving gemtuzumab and the patient provided contraceptive counseling on potential risks vs. benefits of taking gemtuzumab if patient were to become pregnant.
- ☐ Advise females of reproductive potential to use effective contraception during treatment and for at least 6 months after their last dose.
- ☐ Advise males with female partners of reproductive potential to use effective contraception during treatment and for at least 3 months after their last dose.
- ☐ Advise women not to breastfeed during treatment with gemtuzumab and for at least 1 month after last dose.

Dosage and Administration

- Refer to Product Information for dosing, dose modifications and administration details.
- Premedication should include:
  - Acetaminophen 650 mg PO and diphenhydramine 50 mg PO or IV given **1 hour prior** to gemtuzumab
  - AND methylprednisolone 1 mg/kg (or equivalent dose of alternative corticosteroid) within **30 min. prior** to gemtuzumab
  - Additional doses of acetaminophen and diphenhydramine may be administered every 4 hours after the initial pre-treatment dose
  - Repeat methylprednisolone or equivalent corticosteroid for any sign of infusion reaction during infusion or within 4 hours afterwards
- Use appropriate measure to prevent Tumor Lysis Syndrome (TLS).

Monitoring

- ALT, AST, total bilirubin and alkaline phosphatase should be checked prior to each dose
- Monitor for signs/symptoms of Veno-Occlusive Disease (VOD) following treatment with gemtuzumab
- TLS parameters, for those at risk
- Infusion-related reactions can occur during or within 24 hours following a dose of gemtuzumab; pre-medicate prior to each infusion; monitor vital signs frequently during the infusion; continue monitoring for at least 1 hour following the infusion or until signs/symptoms completely resolve.
- CBC prior to each dose and frequently throughout treatment until resolution of cytopenias; monitor for signs/symptoms of bleeding. Of note, cytopenias can be prolonged.
- ECG and electrolytes prior to the start of therapy and as needed throughout if patient has a history or predisposition for QTc prolongation or are taking medications known to prolong the QT interval
- Pregnancy test (in women of childbearing potential) at baseline

Issues for Consideration

- **FDA-approved indication.** Gemtuzumab is approved for the treatment of newly-diagnosed CD33-positive AML in adults. It is also indicated for the treatment of relapsed or refractory CD33-positive AML.
- **Hyperleukocytosis**. It is recommended that these patients receive cytoreduction prior to initiating gemtuzumab.
- **Off-label use in acute promyelocytic leukemia.** Patients with high risk APL (defined as WBC count > 10K) treated with gemtuzumab in combination with ATRA and ATO have noted improved responses without the additional risk of cardiotoxicity from anthracycline therapy. It is unclear if this combination provides a greater response than the addition of an anthracycline, as they were not compared.
- **Hepatotoxicity**. A boxed warning highlights the risk of VOD or SOS, especially in adult patients who received higher doses of gemtuzumab as monotherapy, those with mod/severe hepatic impairment at baseline, treated with gemtuzumab prior to or post-HSCT. ALFA-0701 included a 2-month interval between last dose of gemtuzumab and HSCT.
- **Bleed risk**. Gemtuzumab can cause prolonged thrombocytopenia, which can increase bleed risk. Evaluate blood counts prior to each dose and throughout therapy; monitor patients for bleeding

- **QT interval prolongation.** QT prolongation has been associated with calicheamicin. Evaluate patient risk of QT interval prolongation prior to gemtuzumab initiation and monitor appropriately
- **Adverse-risk cytogenetics.** Patients with adverse-risk cytogenetics did not have improvement in EFS. For patients being treated with gemtuzumab in combination with chemotherapy for newly diagnosed disease, when cytogenetic testing results become available, consider whether the potential benefit of continuing treatment with gemtuzumab outweighs the risks for the individual patient.
- **Other FDA-approved targeted therapies**. GO has not been tested in combination with target therapy for specific mutations in AML. For patients with specific mutations such as FLT3 please refer to the CFU for specific target therapy regimens.

Discontinuation Criteria

- Severe infusion reaction or any life-threatening infusion reaction
- Persistent thrombocytopenia and/or neutropenia, if blood counts do not recover within 14 days after hematologic recovery from the previous cycle (or within 14 days following the planned start date of consolidation cycle)
- Evidence of VOD

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