BLINCYTO® (blinatumomab) for injection
35 mcg single-dose vial

BLINCYTO® (blinatumomab) REMS

FDA-REQUIRED REMS SAFETY INFORMATION

Risk of:

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal**
- **Neurological Toxicities, which may be severe, life-threatening or fatal**
- **Preparation and Administration Errors**

July 2017

Dear Pharmacist:

The FDA has required this safety notice as part of the **BLINCYTO® REMS** (**R**isk **E**valuation and **M**itigation **S**trategy) to inform you about the serious risks of BLINCYTO.

BOXED WARNING: Cytokine Release Syndrome

- Serious adverse events that may be associated with CRS included **pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase, increased aspartate aminotransferase, and increased total bilirubin.**
- The highest elevation of cytokines was observed in the first 2 days following start of BLINCYTO infusion.
- Hospitalization is recommended for the first 9 days of the first cycle and the first 2 days of the second cycle.

BOXED WARNING: Neurological Toxicities

- In patients with acute lymphoblastic leukemia (ALL) receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Among patients that experienced a neurologic event, the median time to the first event was within the first 2 weeks of BLINCYTO treatment and the majority of events resolved.
- Grade 3 or higher (severe, life-threatening or fatal) neurological toxicities following initiation of BLINCYTO administration occurred in approximately 13% of patients and included **encephalopathy, convulsions, speech disorders,disturbances in consciousness, confusion and disorientation, and coordination and balance disorders.** The majority of events resolved following interruption of BLINCYTO, but some resulted in treatment discontinuation.

Monitor patients closely for signs and symptoms of these events and interrupt or discontinue dosing of BLINCYTO.

OTHER SERIOUS RISKS: Preparation and Administration Errors

- **It is very important that the instruction for preparation (including admixing) and administration are strictly followed to minimize medication errors (including underdose and overdose).**
- Please note that the recommended dose for BLINCYTO is by patient weight. Patients greater than or equal to 45 kg receive a fixed-dose and for patients less than 45 kg, the dose is calculated using the patient's body surface area (BSA).

Special Considerations to Support Accurate Preparation

- IV Solution Stabilizer is provided and is used to coat the prefilled IV bag prior to addition of reconstituted BLINCYTO.
- Reconstitute BLINCYTO with Sterile Water for Injection, USP, only.
- Aseptic technique must be done in a USP <797> compliant facility and strictly observed when preparing the solution for infusion since BLINCYTO does not contain antimicrobial preservatives.
- Use the specific volumes described in the admixing instructions.
- **Please see the full Prescribing Information for important details on preparation and administration, including storage requirements for BLINCYTO.**

Please see the enclosed non-promotional REMS Fact Sheet, reviewed by the FDA and the full Prescribing Information for more detailed safety information. Additional copies of the Fact Sheet and other important information are available at: www.blincytorems.com.

BLINCYTO is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

REPORTING ADVERSE EVENTS

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. Healthcare Providers should report all suspected adverse events associated with BLINCYTO to the FDA or to Amgen at 1-800-77-AMGEN (1-800-772-6436).

Sincerely,

Isma Benattia, MD, MBE
Vice President, Global Patient Safety & Labeling

AMGEN®