

## 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

December 2014

Dear Pharmacist:

The FDA has required this safety notice as part of the **BLINCYTO™ REMS** (Risk Evaluation and Mitigation Strategy) 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.

#### **BOXED WARNING: Neurological Toxicities**

- In patients receiving BLINCYTO in clinical trials, neurological toxicities have occurred in approximately 50% of patients.
- The median time to onset of any neurological toxicity was 7 days.
- Grade 3 or higher (severe, life-threatening or fatal) neurological toxicities following initiation of BLINCYTO administration occurred in approximately 15% 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).

## 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.blincyto.rems.com](http://www.blincyto.rems.com).

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

## REPORTING ADVERSE EVENTS

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit [www.fda.gov/medwatch](http://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