

BLINCYTO® REMS FACT SHEET FOR HEALTHCARE PROVIDERS

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**

BOXED WARNING

Cytokine Release Syndrome

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®.
- The median time to onset of CRS is 2 days after the start of infusion.
- Manifestations of CRS include **fever, headache, nausea, asthenia, hypotension, increased alanine aminotransferase, increased aspartate aminotransferase, increased total bilirubin, and disseminated intravascular coagulation (DIC)**.
- The manifestations of CRS after treatment with BLINCYTO overlap with those of infusion reactions, capillary leak syndrome (CLS), and hemophagocytic histiocytosis/macrophage activation syndrome (MAS).
- Using all of these terms to define CRS, in clinical trials of BLINCYTO, CRS was reported in 15% of patients with relapsed or refractory acute lymphoblastic leukemia (ALL) and in 7% of patients with minimal residual disease (MRD)-positive ALL.
- Monitor patients for signs or symptoms of these events.
 - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD greater than or equal to 0.1%, hospitalization is recommended for the first 3 days of the first cycle and the first 2 days of the second cycle.
 - In patients treated for relapsed or refractory CD19-positive B-cell precursor ALL, hospitalization is recommended for the first 9 days of the first cycle and the first 2 days of the second cycle.
- Administer corticosteroids for severe or life-threatening CRS.

Neurological Toxicities

- In patients with 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.
- Manifestations of neurological toxicity included cranial nerve disorders.
- 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 BLINCYTO dosing. Advise outpatients on BLINCYTO to contact their healthcare professional if they develop signs or symptoms of these events.

OTHER SERIOUS RISKS:

Preparation and Administration Errors

- Preparation and administration errors have occurred with BLINCYTO treatment.
- Please refer to the updated instructions on the preparation and administration of BLINCYTO in Sections 2.5 and 2.6 of the Prescribing Information. It is very important that the instructions for preparation (including admixing) and administration are strictly followed to minimize medication errors (including underdose or 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. For patients less than 45 kg, the dose is calculated using the patient's body surface area (BSA).
- See Dosage and Administration section of Prescribing Information for detailed safety information.

MORE INFORMATION

For detailed information regarding BLINCYTO including storage, preparation, and administration, it is essential that you read the Prescribing Information for BLINCYTO.

INDICATION

BLINCYTO is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of adults and children with 1) CD19-positive B-cell precursor ALL in first or second complete remission with MRD greater than or equal to 0.1% and 2) relapsed or refractory CD19-positive B-cell precursor ALL.

WHAT IS THE BLINCYTO® REMS?

A REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary to ensure that the benefits of BLINCYTO outweigh its risks. The purpose of the BLINCYTO REMS is to inform Healthcare Providers of the risks of serious neurological toxicities, cytokine release syndrome, and preparation and administration errors. This Fact Sheet is required by the FDA as part of the BLINCYTO REMS program.

Please visit www.blincyto.rems.com for further information and resources.

This Fact Sheet does not contain the complete safety profile for BLINCYTO. Please refer to the full Prescribing Information, including **BOXED WARNINGS** and Medication Guide.

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).