



BLINCYTO® (blinatumomab) Risk Evaluation and Mitigation Strategy (REMS)

What is the BLINCYTO® REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a program to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

The purpose of the BLINCYTO REMS is to inform Healthcare Providers about the following serious risks:

BOXED WARNING: Cytokine Release Syndrome

- Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Manifestations of CRS include **fever, headache, nausea, asthenia, hypotension, increased alanine aminotransferase, increased aspartate aminotransferase, increased total bilirubin, and disseminated intravascular coagulation (DIC)**.
- Manifestations of CRS after treatment with BLINCYTO overlap with those of infusion reactions, capillary leak syndrome (CLS), and hemophagocytic histiocytosis/macrophage activation syndrome (MAS).
- The median time to onset of CRS is 2 days after the start of infusion.
- Monitor patients for signs or symptoms of these events.
 - In patients treated for CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (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 acute 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.

BOXED WARNING: 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 dosing of BLINCYTO. Advise outpatients on BLINCYTO to contact their healthcare professional if they develop signs or symptoms of these events.

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).

BLINCYTO Fact Sheet:

A non-promotional REMS Fact Sheet reviewed by the FDA, with more detailed information on the serious risks associated with BLINCYTO is available in the "Materials for Healthcare Providers" section above.

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.

You are encouraged to report negative side effects of BLINCYTO to Amgen at 1-800-77-AMGEN (1-800-772-6436) and/or the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

Materials for Healthcare Providers

BLINCYTO® REMS Letter for Healthcare Providers

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BLINCYTO® REMS Letter for Hospital and Home Healthcare Pharmacists

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BLINCYTO® REMS Fact Sheet for Healthcare Providers

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