



## 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

- 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 receiving BLINCYTO in clinical trials, neurological toxicities have occurred in approximately 64% of patients.
- The median time to onset of any neurological toxicity was 4 days.
- Grade 3 or higher (severe, life-threatening or fatal) neurological toxicities following initiation of BLINCYTO administration occurred in approximately 17% 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.**

### Preparation and Administration Errors

- Preparation and administration errors have occurred with BLINCYTO treatment.
- **It is very important that the instructions 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).

### 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 Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (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](http://www.fda.gov/medwatch) or call 1-800-FDA-1088

### Materials for Healthcare Providers

#### BLINCYTO® REMS Letter for Healthcare Providers

[Download PDF](#)

#### BLINCYTO® REMS Letter for Hospital and Home Healthcare Pharmacists

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#### BLINCYTO® REMS Fact Sheet for Healthcare Providers

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August 2016

## IMPORTANT DRUG WARNING

**Subject: New Safety Information for BLINCYTO (blinatumomab) - Risk of Pancreatitis**

Dear Health Care Provider:

The purpose of this letter is to inform you of important safety information for BLINCYTO, a bispecific CD19-directed CD3 T-cell engager approved for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials.

### **Risk of Pancreatitis with use of BLINCYTO**

- As of February 2016, events of pancreatitis, some life-threatening or fatal, have been reported in 10 patients out of approximately 2000 patients from clinical trials and the post-marketing setting. High-dose steroid therapy may have contributed, in some cases, to the pancreatitis.
- Although in some cases there were confounding medications and occasionally missing information, the association of pancreatitis with BLINCYTO administration, the frequency and seriousness of events, and a positive dechallenge/positive rechallenge case warrant an update to the BLINCYTO prescribing information.

### **Prescriber Action**

- Evaluate patients who develop signs and symptoms of pancreatitis.
- Management of pancreatitis may require either temporary interruption or discontinuation of BLINCYTO.

### **Action being taken by Amgen**

Amgen has worked with the FDA to include language regarding pancreatitis in Section 5 Warnings and Precautions and Section 6 Adverse Reactions of the BLINCYTO prescribing information. The medication guide has also been updated to include this new information.

Additional information about this risk is provided in the remainder of this letter.

### **Further information on the safety concern**

In clinical trials, 6 cases suggestive of pancreatitis were reported in patients receiving BLINCYTO. Two cases described increase in pancreatic enzymes (such as increased lipase) with associated symptoms. Four cases (3 non-serious and 1 serious) reported adverse events of pancreatitis. The 1 serious event of pancreatitis was reported in a patient with elevations of lipase and total bilirubin before treatment with BLINCYTO; the event did not resolve with the discontinuation of BLINCYTO.

In the post-marketing setting, 4 cases reported events of pancreatitis (n=2), acute pancreatitis (n=1), and necrotizing pancreatitis (n=1). The case of necrotizing pancreatitis, with a fatal outcome, was reported in

a patient receiving dexamethasone and prior treatment with multiple chemotherapy regimens. In this patient, increase in lipase levels coincided with the dexamethasone dosing during the administration of BLINCYTO; the patient's course was complicated by colitis and sepsis. In one of the cases that reported an event of pancreatitis, the symptoms subsided upon temporary withdrawal of BLINCYTO and recurred after resuming treatment (positive dechallenge/positive rechallenge). The remaining post-marketing cases described 1 patient with an event of pancreatitis in the context of leukemic infiltration; and 1 patient with an event of acute pancreatitis in the setting of concurrent appendicitis.

### **Reporting Adverse Events**

Health care providers and patients are encouraged to report adverse events in patients taking BLINCYTO to Amgen at 1-800-77-AMGEN (1-800-772-6436). 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.

You may also contact our medical information department at 1-800-77-AMGEN (1-800-772-6436) if you have any questions about the information contained in this letter or the safe and effective use of BLINCYTO.

This letter is not intended as a complete description of the benefits and risks related to the use of BLINCYTO. Please refer to the enclosed full prescribing information (and medication guide).

Sincerely,

Paul Eisenberg, MD  
Senior Vice President of Global Medical and Chief Medical Officer

Enclosure(s): BLINCYTO Full Prescribing Information, Medication Guide