

# Risk Evaluation and Mitigation Strategy (REMS) Document

## BLINCYTO® (blinatumomab) REMS Program

### I. Administrative Information

Application Number: BLA 125557  
Application Holder: Amgen, Inc.  
Initial REMS Approval: 12/2014  
Most Recent REMS Update: Month/2021

### II. REMS Goals

The goals of the BLINCYTO REMS are to mitigate the risk of cytokine release syndrome which may be life-threatening or fatal; the risk of neurological toxicities which may be severe, life-threatening, or fatal; and the risk of preparation and administration errors associated with use of BLINCYTO by:

1. Informing healthcare providers about the risk of cytokine release syndrome which may be life-threatening or fatal
2. Informing healthcare providers about the risk of neurological toxicities which may be severe, life-threatening, or fatal
3. Informing pharmacists, who will prepare and dispense BLINCYTO, and nurses, who will administer BLINCYTO, about the risk of preparation and administration errors associated with use of BLINCYTO.

### III. REMS Requirements

**To inform healthcare providers about the REMS Program and the risks and safe use of BLINCYTO, Amgen must disseminate REMS communication materials according to the table below:**

Target Audience	Communication Materials & Dissemination Plans
Healthcare providers including oncologists, oncology physician assistants, oncology nurse practitioners, hematologists, oncology nurses, home healthcare oncology nurses, and infusion nurses; healthcare providers who have prescribed BLINCYTO within the previous 12 months from the approval of this REMS modification; healthcare providers who are likely to prescribe or administer BLINCYTO	<p>REMS Letter: <a href="#">REMS Letter for Healthcare Provider</a> or <a href="#">REMS Letter for Professional Societies</a> with attachment <a href="#">Fact Sheet for Providers</a></p> <ol style="list-style-type: none"><li>1. Email within 60 calendar days of approval of the REMS modification (Month/2021) and again 12 months later.<ol style="list-style-type: none"><li>a. Send by mail within 30 calendar days of the date the first email was sent if a healthcare provider's email address is not available or the email is undeliverable.</li><li>b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened.</li><li>c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened.</li></ol></li><li>2. Make available via a link from the BLINCYTO REMS Program Website.</li><li>3. Disseminate through field-based sales and medical representatives for 6 months from approval of the REMS modification (Month/2021).</li><li>4. Disseminate to professional societies within 60 calendar days of the approval of the REMS modification (Month/2021), again 12 months later and request the letter or content be provided to their members.</li><li>5. Disseminate at Professional Meetings for 6 months from approval of the REMS modification (Month/2021).</li></ol>

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**Target Audience****Communication Materials & Dissemination Plans**

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**Fact Sheet for Providers**

1. Disseminate and prominently display at Professional Meetings where Amgen has a presence for 6 months from approval of the REMS modification (Month/2021).
  2. Disseminate through field-based sales and medical representatives during the initial or follow-up discussion with healthcare providers for 6 months from approval of the REMS modification (Month/2021). Field-based sales or medical representatives to orally review the risk messages contained in the [Fact Sheet for Providers](#) during the visit with the healthcare provider.
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Hospital-based pharmacists and home healthcare pharmacists

REMS Letter: [REMS Letter for Hospital and Home Healthcare Pharmacists](#) or [REMS Letter for Professional Societies](#) with attachment [Fact Sheet for Providers](#)

1. Email within 60 calendar days of the approval of the REMS modification (Month/2021) and again 12 months later.
  - a. Send by mail within 30 calendar days of the date the first email was sent if a pharmacist's email address is not available or the email is undeliverable.
  - b. Send a second email within 30 calendar days of the date the first email was sent if the first email is marked as unopened.
  - c. Send by mail within 30 calendar days of the date the second email was sent if the second email is marked as unopened.
2. Make available via a link from the BLINCYTO REMS Program Website.
3. Disseminate through field-based sales and medical representatives for 6 months from approval of the REMS modification (Month/2021).
4. Disseminate to professional societies within 60 calendar days of the approval of the REMS modification (Month/2021), again 12 months later, and request the letter or content be provided to their members.
5. Disseminate at Professional Meetings for 6 months from approval of the REMS modification (Month/2021).

**Fact Sheet for Providers**

1. Disseminate and prominently display at Professional Meetings where Amgen has a presence for 6 months from approval of the REMS modification (Month/2021).
  2. Disseminate through field-based sales and medical representatives during the initial or follow-up discussion with healthcare providers for 6 months from approval of the REMS modification (Month/2021). Field-based sales or medical representatives to orally review the risk messages contained in the [Fact Sheet for Providers](#) during the visit with the healthcare provider.
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**REMS Program Website**

1. Include all currently approved REMS materials, Prescribing Information, and Medication Guide.
  2. Include a prominent REMS-specific link to the BLINCYTO REMS Program website. The BLINCYTO REMS Program website must not link back to the promotional product website.
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**Target Audience****Communication Materials & Dissemination Plans**

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3. Continue for 3 years from approval of the REMS modification (Month/2021).
  4. Update all information within 60 calendar days from approval of the REMS modification (Month/2021).
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**IV. REMS Assessment Timetable**

Amgen must submit REMS Assessments at 18 months, 3 years, 5 years, and 7 years from the date of the initial REMS approval (12/03/2014). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Amgen must submit each assessment so that it will be received by the FDA on or before the due date.

**V. REMS Materials**

The following materials are part of the BLINCYTO REMS:

**Communication Materials**

1. [REMS Letter for Healthcare Provider](#)
2. [REMS Letter for Hospital and Home Healthcare Pharmacists](#)
3. [REMS Letter for Professional Societies](#)
4. [Fact Sheet for Providers](#)

**Other Materials**

5. [REMS Program Website](#)

From: Amgen Inc.  
To: <Healthcare Provider email>  
Subject: FDA-Required Updated REMS Safety Information for BLINCYTO®



**FDA-REQUIRED UPDATED  
REMS SAFETY INFORMATION**

## BLINCYTO® (blinatumomab) REMS

**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

Month 2021

Dear Healthcare Provider:

The Food and Drug Administration (FDA) has required this safety notice as part of the BLINCYTO® REMS (Risk Evaluation and Mitigation Strategy) to highlight risk information about cytokine release syndrome and neurological toxicities for BLINCYTO. In addition, Amgen would like to highlight updated preparation and administration instructions.

Please see the non-promotional [REMS Fact Sheet](#) for more detailed safety information.

### **BOXED WARNING: Cytokine Release Syndrome**

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

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

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Manifestations of neurological toxicity included cranial nerve disorders.

### **OTHER SERIOUS RISKS: Preparation and Administration Errors**

-  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 see the 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](http://www.blincytoREMS.com).

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.

To review the Prescribing Information and Medication Guide, see links below:

[Prescribing Information](#)

[Medication Guide](#)

### **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,

Fatima Bhayat MD MPH PhD FPPM  
Vice President, Global Patient Safety

BLINCYTO® is a registered trademark of Amgen Inc.  
©2018-2021 Amgen Inc. All rights reserved.



## BLINCYTO<sup>®</sup> (blinatumomab) REMS

### 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

Month 2021

Dear Healthcare Provider:

The Food and Drug Administration (FDA) has required this safety notice as part of the BLINCYTO<sup>®</sup> REMS (Risk Evaluation and Mitigation Strategy) to highlight risk information about **cytokine release syndrome and neurological toxicities** for BLINCYTO. In addition, Amgen would like to highlight updated preparation and administration instructions.

### **BOXED WARNING: Cytokine Release Syndrome**

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

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

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Manifestations of neurological toxicity included cranial nerve disorders.

### **OTHER SERIOUS RISKS: Preparation and Administration Errors**

- **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 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 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.

## 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,

Fatima Bhayat MD MPH PhD FFPM  
Vice President, Global Patient Safety

From: Amgen Inc.  
To: <Pharmacist Email>  
Subject: FDA-Required Updated REMS Safety Information for BLINCYTO®



**FDA-REQUIRED UPDATED  
REMS SAFETY INFORMATION**

## BLINCYTO® (blinatumomab) REMS

**Risk of:**

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

Month 2021

Dear Pharmacist:

The Food and Drug Administration (FDA) has required this safety notice as part of the BLINCYTO® REMS (Risk Evaluation and Mitigation Strategy) to remind you of the serious risk of preparation and administration errors and highlight risk information about cytokine release syndrome and neurological toxicities for BLINCYTO. In addition, Amgen would like to highlight updated preparation and administration instructions.

Please see the non-promotional [REMS Fact Sheet](#) for more detailed safety information.

### Preparation and Administration Errors



- 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).

### Special Considerations to Support Accurate Preparation

- Intravenous (IV) Solution Stabilizer is provided and is used to coat the IV bag prior to addition of reconstituted BLINCYTO.
- Reconstitute BLINCYTO with preservative-free 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.

### BOXED WARNING: Cytokine Release Syndrome

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

### BOXED WARNING: Neurological Toxicities

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
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To review the Prescribing Information and Medication Guide, see links below:

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[Medication Guide](#)

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Sincerely,

Fatima Bhayat MD MPH PhD FFPM  
Vice President, Global Patient Safety

## BLINCYTO<sup>®</sup> (blinatumomab) REMS

### Risk of:

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

Month 2021

Dear Pharmacist:

The Food and Drug Administration (FDA) has required this safety notice as part of the **BLINCYTO<sup>®</sup> REMS (Risk Evaluation and Mitigation Strategy)** to remind you of the serious risk of **preparation and administration errors** and highlight risk information about **cytokine release syndrome and neurological toxicities** for BLINCYTO. In addition, Amgen would like to highlight updated preparation and administration instructions.

### Preparation and Administration Errors

Note

- **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).

### Special Considerations to Support Accurate Preparation

- Intravenous (IV) Solution Stabilizer is provided and is used to coat the IV bag prior to addition of reconstituted BLINCYTO.
- Reconstitute BLINCYTO with preservative-free 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.**

## **BOXED WARNING: Cytokine Release Syndrome**

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

## **BOXED WARNING: Neurological Toxicities**

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Manifestations of neurological toxicity included cranial nerve disorders.

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](http://www.blincytoREMS.com).

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.

## **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,

Fatima Bhayat MD MPH PhD FFPM  
Vice President, Global Patient Safety

From: Amgen Inc.  
To: <Professional Society email>  
Subject: FDA-Required Updated REMS Safety Information for BLINCYTO®



**FDA-REQUIRED UPDATED  
REMS SAFETY INFORMATION**

## BLINCYTO® (blinatumomab) REMS

**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

Month 2021

Dear [name]:

The Food and Drug Administration (FDA) has required this safety notice as part of the BLINCYTO® REMS (Risk Evaluation and Mitigation Strategy) to be distributed to the [insert Professional Society Name] to highlight safety information about **cytokine release syndrome and neurological toxicities**. In addition, Amgen would like to highlight updated preparation and administration instructions. Amgen requests that you distribute the information to your members, informing them about the serious risks of BLINCYTO.

### BOXED WARNING: Cytokine Release Syndrome

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

### BOXED WARNING: Neurological Toxicities

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Manifestations of neurological toxicity included cranial nerve disorders.

### OTHER SERIOUS RISKS: Preparation and Administration Errors

-  • **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 see the 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](http://www.blincytoREMS.com).

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.

Sincerely,

Fatima Bhayat MD MPH PhD FPPM  
Vice President, Global Patient Safety

## BLINCYTO<sup>®</sup> (blinatumomab) REMS

### 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**

Month 2021

Dear <name>:

The Food and Drug Administration (FDA) has required this safety notice as part of the **BLINCYTO<sup>®</sup> REMS (Risk Evaluation and Mitigation Strategy)** to be distributed to the <insert Professional Society Name> to highlight safety information about **cytokine release syndrome and neurological toxicities**. In addition, Amgen would like to highlight updated preparation and administration instructions. Amgen requests that you distribute the information to your members, informing them about the serious risks of BLINCYTO.

### **BOXED WARNING: Cytokine Release Syndrome**

- CRS, which may be life-threatening or fatal, occurred in patients receiving BLINCYTO.
- Monitor patients for signs or symptoms of CRS.
- BLINCYTO is approved for the treatment of 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% in adults and children and for the treatment of relapsed or refractory CD19-positive B-cell precursor ALL in adults and children.
  - In patients treated for CD19-positive B-cell precursor ALL in first or second complete remission with MRD, 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.

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

- In patients with ALL receiving BLINCYTO in clinical studies, neurological toxicities have occurred in approximately 65% of patients.
- Manifestations of neurological toxicity included cranial nerve disorders.

### **OTHER SERIOUS RISKS: Preparation and Administration Errors**

- **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 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](http://www.blincytoREMS.com).

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.

Sincerely,

Fatima Bhayat MD MPH PhD FFPM  
Vice President, Global Patient Safety

## 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](http://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](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).



## 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](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

• [Download PDF](#)

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

• [Download PDF](#)

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