BLINCYTO® (blinatumomab) for injection 35 mcg single-use vial

The BLINCYTO®

Treatment Journey

Considerations for patient's care—from the first in-hospital infusion through the transition to the next infusion(s).

INDICATIONS

BLINCYTO® (blinatumomab) is indicated for the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients one month and older with:

- Philadelphia chromosome-negative disease in the consolidation phase of multiphase chemotherapy
- Minimal residual disease (MRD) greater than or equal to 0.1% in first or second complete remission
- Relapsed or refractory disease

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® and treat with corticosteroids as recommended.**
- **Neurological toxicities, including immune effector cell-associated neurotoxicity syndrome (ICANS) which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® as recommended.**

Contraindications

BLINCYTO® is contraindicated in patients with a known hypersensitivity to blinatumomab or to any component of the product formulation.

Warnings and Precautions

- **Cytokine Release Syndrome (CRS):** 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 and the median time to resolution of CRS was 5 days among cases that resolved. Closely monitor and advise patients to contact their healthcare professional for signs and symptoms of serious adverse events such as fever, headache, nausea, asthenia, hypotension, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), 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 R/R ALL, in 7% of patients with MRD-positive ALL, and in 16% of patients receiving BLINCYTO® cycles in the consolidation phase of therapy. If severe CRS occurs, interrupt BLINCYTO® until CRS resolves. Discontinue BLINCYTO® permanently if life-threatening CRS occurs. Administer corticosteroids for severe or life-threatening CRS.

Please click here for BLINCYTO® full Prescribing Information, including BOXED WARNINGS, and see Important Safety Information throughout.

Considerations for helping guide patients through their BLINCYTO® treatment journey

Discharge planning early on can be an important factor in a patient's smooth transition to outpatient treatment.

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Key considerations for your healthcare team for care coordination

Patient treatment journeys may vary between infusions. Amgen® SupportPlus may be able to provide support along the way.

1 PRE-ADMISSION CONSIDERATIONS

Doctor decides patient is suitable for BLINCYTO.

Note: Consider when to start BLINCYTO and align with hospital discharge. Develop a multidisciplinary team for care of patient.

Pre-Admission Details for Key Staff

Nurse Manager, Pharmacy Director, Discharge Planner/Benefits Coordinator

Ambulatory Pump Supplier Considerations

When choosing an infusion pump services provider, some considerations, among other things, include:

- Pump rental, maintenance, and support
- Treatment compatibility
- Back-up pump availability

Pre-Admission Details

- ✓ **Confirm** patient's benefits coverage and coordinate payer pre-approval for discharge sites of care options, and/or submit for prior authorization requirements ●
- ✓ **Assess** and discuss outpatient discharge options based on benefits coverage with patient to determine feasibility of home health care vs ambulatory clinic ●●
- ✓ **Set up** a discharge plan with outpatient clinic or home infusion agency

CONFIRM INFUSION LOCATION TO CHECK COVERAGE

This may be a home infusion or an infusion at an outpatient clinic near the patient's home. The patient's benefits coverage can be checked to see what they're eligible for. It's also helpful to be able to walk them through what they can expect.

Amgen® SupportPlus resources are available to help support your patient's transition of care and are color coded touchpoints below for quick reference.

The patient journey outlined in this resource with the Amgen SupportPlus touchpoints assumes a hypothetical patient journey, inclusive of patient diagnosis, and enrollment in Amgen SupportPlus. Each patient journey is different, and all touchpoints here are for illustrative purposes. Amgen SupportPlus may provide support to patients and office staff beyond the touchpoints outlined here.

Amgen® Patient Navigator ●

The Amgen Patient Navigator is part of your Amgen SupportPlus support team and will be with you as your patient starts BLINCYTO.* The navigator is a single point of contact to help answer questions about:

- Access and reimbursement
- Navigating treatment logistics
- Supplemental resources as patients transition from hospital to outpatient care on BLINCYTO.

* The Amgen Patient Navigator is not part of a patient's treatment team and does not provide medical advice or case management services. The Amgen Patient Navigator does not administer Amgen medications. Patients should always consult their healthcare provider regarding medical decisions or treatment concerns.

Amgen SupportPlus Representatives ●

Our Amgen SupportPlus Representatives can assist with issues around patient coverage, prior authorizations, co-pay programs, and more.

Amgen Therapy Locator™ ●

Amgen Therapy Locator is a tool to help patients and healthcare providers find the nearest site of care for Amgen therapies.

Treatment Referral Form ●

This form needs to be completed and submitted to the Home Infusion Agency with the patient face sheet and supplemental relevant clinical notes.

Amgen® Nurse Partners will be available to forward and connect patient and HCP queries to the Patient Navigator.†
Amgen® Access Specialists can answer questions directly, will inform the Patient Navigator, and transfer the information over to support moving forward.

† Amgen Nurse Partners are only available to patients that are prescribed certain Amgen products. They are not part of your patient's treatment team and do not provide medical advice, nursing, or case management services. Amgen Nurse Partners will not inject patients with Amgen medications. Patients should always consult their healthcare provider regarding medical decisions or treatment concerns.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **Neurological Toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome:** BLINCYTO® can cause serious or life-threatening neurologic toxicity, including ICANS. The incidence of neurologic toxicities in clinical trials was approximately 65%. The median time to the first event was within the first 2 weeks of BLINCYTO® treatment. The most common (≥ 10%) manifestations of neurological toxicity were headache and tremor. Grade 3 or higher neurological toxicities occurred in approximately 13% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. Manifestations of neurological toxicity included cranial nerve disorders. The majority of neurologic toxicities resolved following interruption of BLINCYTO®, but some resulted in treatment discontinuation.

Please click here for BLINCYTO® full Prescribing Information, including BOXED WARNINGS, and see Important Safety Information throughout.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

The incidence of signs and symptoms consistent with ICANS in clinical trials was 7.5%. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. There is limited experience with BLINCYTO® in patients with active ALL in the central nervous system (CNS) or a history of neurologic events. Patients with a history or presence of clinically relevant CNS pathology were excluded from clinical studies. Patients with Down Syndrome over the age of 10 years may have a higher risk of seizures with BLINCYTO® therapy.

Monitor patients for signs and symptoms of neurological toxicities, including ICANS, and interrupt or discontinue BLINCYTO® as outlined in the PI. Advise outpatients to contact their healthcare professional if they develop signs or symptoms of neurological toxicities.

Considerations for helping guide patients through their BLINCYTO® treatment journey

Discharge planning early on can be an important factor in a patient's smooth transition to outpatient treatment.

Key considerations for your healthcare team for care coordination

Patient treatment journeys may vary between infusions. Amgen® SupportPlus may be able to provide support along the way.

1 PRE-ADMISSION CONSIDERATIONS

Doctor decides patient is suitable for BLINCYTO.

Note: Consider when to start BLINCYTO and align with hospital discharge. Develop a multidisciplinary team for care of patient.

Pre-Admission Details for Key Staff

Nurse Manager, Pharmacy Director, Discharge Planner/Benefits Coordinator

Ambulatory Pump Supplier Considerations

When choosing an infusion pump services provider, some considerations, among other things, include:

- Pump rental, maintenance, and support
- Treatment compatibility
- Back-up pump availability

Pre-Admission Details

- ✓ **Confirm** patient's benefits coverage and coordinate payer pre-approval for discharge sites of care options, and/or submit for prior authorization requirements ●
- ✓ **Assess** and discuss outpatient discharge options based on benefits coverage with patient to determine feasibility of home health care vs ambulatory clinic ●●
- ✓ **Set up** a discharge plan with outpatient clinic or home infusion agency

CONFIRM INFUSION LOCATION TO CHECK COVERAGE

This may be a home infusion or an infusion at an outpatient clinic near the patient's home. The patient's benefits coverage can be checked to see what they're eligible for. It's also helpful to be able to walk them through what they can expect.

WHERE WILL THEY INFUSE NEXT?

Will they stay in-patient, discharge to outpatient, or do home infusion? This conversation happens here to help determine next steps. This is also where inpatient administration happens, as well as a monitoring period for CRS and neurological toxicities.

2 STARTING TREATMENT

Patient is admitted to the inpatient unit.

Starting Treatment Details for Key Staff

Oncologist, Clinical Pharmacist, Nurse

Starting Treatment Details

- ✓ **Confirm** prescriber's orders, labs, pre-medication, and supplies are ready (pump, tubing, etc)
- ✓ **Coordinate** with pharmacy for start time and bag changes during hospitalization
- ✓ **Prepare** dosing administration plan and confirm staff for infusion bag changes
- ✓ **Provide** education to the patient and caregiver on what to expect during treatment journey

3 BEFORE DISCHARGE

Prepare for hospital discharge and continuation of care with multidisciplinary team.

Before Discharge Details for Key Staff

Case Worker, Home Care Coordinator, Discharge Planner, Home Health Liaison

Before Discharge Details

- ✓ **Coordinate** with discharge site of care to determine coverage and support prior authorization process ●●●
- ✓ **Verify** discharge site of care is ready to administer BLINCYTO (drug/staff/supplies)
- ✓ **Educate** caregiver on what is needed after discharge

Outpatient Key Staff

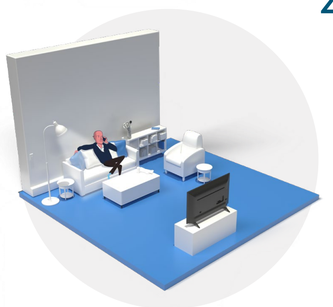
Outpatient RN, Pharmacist

Outpatient

- ✓ **Make** sure outpatient site of care arrangements are in place
- ✓ **Verify** proximity to clinic and confirm potential transportation and lodging needs
- ✓ **Support** accurate Billing and Coding coordination between sites ●

4 AFTER DISCHARGE

Patient treatment continues at outpatient clinic or home with home infusion.



Home Care Key Staff

Home Health Nursing, Home Infusion Specialty Pharmacy Services, Clinical Care Liaison

Home (optional treatment)

- ✓ **Help** educate on medication questions
- ✓ **Schedule** home health care visits and ensure proper medication storage
- ✓ **Ensure** home infusion claims are properly submitted under the right coverage benefits ●

QUICK REFERENCE KEY:

Amgen Patient Navigator* | Amgen SupportPlus Representatives Benefits Investigation/Financial Assistance | Amgen Therapy Locator™ | Treatment Referral Form

Please refer to the full Prescribing Information for dosing, monitoring, and hospitalization requirements. The patient journey outlined in this resource assumes a hypothetical patient journey; each patient journey is different and all touchpoints here are for illustrative purposes.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **Neurological Toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome:** BLINCYTO® can cause serious or life-threatening neurologic toxicity, including ICANS. The incidence of neurologic toxicities in clinical trials was approximately 65%. The median time to the first event was within the first 2 weeks of BLINCYTO® treatment. The most common (≥ 10%) manifestations of neurological toxicity were headache and tremor. Grade 3 or higher neurological toxicities occurred in approximately 13% of patients, including encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. Manifestations of neurological toxicity included cranial nerve disorders. The majority of neurologic toxicities resolved following interruption of BLINCYTO®, but some resulted in treatment discontinuation.

Please click here for BLINCYTO® full Prescribing Information, including BOXED WARNINGS, and see Important Safety Information throughout.

BLINCYTO contains BOXED WARNINGS for CRS and neurological toxicities, including ICANS, which may be life-threatening or fatal, and occurred in patients receiving BLINCYTO. Interrupt or discontinue BLINCYTO as recommended. Additionally, for CRS, treat with corticosteroids as recommended.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise patients of the risk of CRS and infusion reactions, as well as the risk of neurological toxicities, including ICANS, and to contact their healthcare professional for signs and symptoms:

- CRS or infusion reactions: pyrexia, fatigue, nausea, vomiting, chills, hypotension, rash, and wheezing
- Neurological toxicities, including ICANS: convulsions, speech disorders, and confusion

Please see the BLINCYTO full Prescribing Information and Medication Guide for additional Important Safety Information, Dosing & Administration information, and additional considerations for AEs, including BOXED WARNINGS.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **Infections:** Approximately 25% of patients receiving BLINCYTO® in clinical trials experienced serious infections such as sepsis, pneumonia, bacteremia, opportunistic infections, and catheter-site infections, some of which were life-threatening or fatal. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment. Monitor patients for signs or symptoms of infection and treat appropriately, including interruption or discontinuation of BLINCYTO® as needed.
- **Tumor Lysis Syndrome (TLS),** which may be life-threatening or fatal, has been observed. Preventive measures, including pretreatment nontoxic cytoreduction and on-treatment hydration, should be used during BLINCYTO® treatment. Monitor patients for signs and symptoms of TLS and interrupt or discontinue BLINCYTO® as needed to manage these events.
- **Neutropenia and Febrile Neutropenia,** including life-threatening cases, have been observed. Monitor appropriate laboratory parameters (including, but not limited to, white blood cell count and absolute neutrophil count) during BLINCYTO® infusion and interrupt BLINCYTO® if prolonged neutropenia occurs.
- **Effects on Ability to Drive and Use Machines:** Due to the possibility of neurological events, including seizures and ICANS, patients receiving BLINCYTO® are at risk for loss of consciousness, and should be advised against driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while BLINCYTO® is being administered.

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AMGEN Support+

Amgen SupportPlus offers personalized support.

From a dedicated Patient Navigator to financial support, resources, and more—throughout your patient's journey, Amgen SupportPlus is ready to help.

Scan the QR code to learn more about Amgen SupportPlus.

CALL 866-264-2778 Monday to Friday, 9:00 AM to 8:00 PM ET, or visit **AmgenSupportPlus.com.**

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **Elevated Liver Enzymes:** Transient elevations in liver enzymes have been associated with BLINCYTO® treatment with a median time to onset of 3 days. In patients receiving BLINCYTO®, although the majority of these events were observed in the setting of CRS, some cases of elevated liver enzymes were observed outside the setting of CRS, with a median time to onset of 19 days. Grade 3 or greater elevations in liver enzymes occurred in approximately 7% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients. Monitor ALT, AST, gamma-glutamyl transferase, and total blood bilirubin prior to the start of and during BLINCYTO® treatment. BLINCYTO® treatment should be interrupted if transaminases rise to > 5 times the upper limit of normal (ULN) or if total bilirubin rises to > 3 times ULN.
- **Pancreatitis:** Fatal pancreatitis has been reported in patients receiving BLINCYTO® in combination with dexamethasone in clinical trials and the post-marketing setting. Evaluate patients who develop signs and symptoms of pancreatitis and interrupt or discontinue BLINCYTO® and dexamethasone as needed.
- **Leukoencephalopathy:** Although the clinical significance is unknown, cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO®, especially in patients previously treated with cranial irradiation and antileukemic chemotherapy.
- **Preparation and administration** errors have occurred with BLINCYTO® treatment. Follow instructions for preparation (including admixing) and administration in the PI strictly to minimize medication errors (including underdose and overdose).
- **Immunization:** Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to the start of BLINCYTO® treatment, during treatment, and until immune recovery following last cycle of BLINCYTO®.
- **Benzyl Alcohol Toxicity in Neonates:** Serious adverse reactions, including fatal reactions and the "gasping syndrome," have been reported in very low birth weight (VLBW) neonates born weighing less than 1500 g, and early preterm neonates (infants born less than 34 weeks gestational age) who received intravenous drugs containing benzyl alcohol as a preservative. Early preterm VLBW neonates may be more likely to develop these reactions because they may be less able to metabolize benzyl alcohol. Use the preservative-free preparations of BLINCYTO® where possible in neonates. When prescribing BLINCYTO® (with preservative) for neonatal patients, consider the combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative), other products containing benzyl alcohol or other excipients (e.g., ethanol, propylene glycol) which compete with benzyl alcohol for the same metabolic pathway. Monitor neonatal patients receiving BLINCYTO® (with preservative) for new or worsening metabolic acidosis. The minimum amount of benzyl alcohol at which serious adverse reactions may occur in neonates is not known. The BLINCYTO® 7-Day bag (with preservative) contains 7.4 mg of benzyl alcohol per mL
- **Embryo-Fetal Toxicity:** Based on its mechanism of action, BLINCYTO® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with BLINCYTO® and for 48 hours after the last dose.

Adverse Reactions

- The safety of BLINCYTO® in adult and pediatric patients one month and older with MRD-positive B-cell precursor ALL (n=137), relapsed or refractory B-cell precursor ALL (n=267), and Philadelphia chromosome-negative B cell precursor ALL in consolidation (n=165) was evaluated in clinical studies. The most common adverse reactions (≥ 20%) to BLINCYTO® in this pooled population were pyrexia, infusion-related reactions, headache, infection, musculoskeletal pain, neutropenia, nausea, anemia, thrombocytopenia, and diarrhea.

Dosage and Administration Guidelines

- BLINCYTO® is administered as a continuous intravenous infusion at a constant flow rate using an infusion pump which should be programmable, lockable, non-elastomeric, and have an alarm.
- It is very important that the instructions for preparation (including admixing) and administration provided in the full Prescribing Information are strictly followed to minimize medication errors (including underdose and overdose).

Please click here for BLINCYTO® full Prescribing Information, including BOXED WARNINGS.

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