A resource for nurses and pharmacists

BLINCYTO® Handling Guide

This guide does not take the place of the preparation and reconstitution instructions located in the full Prescribing Information (PI) and Instructions for Use (IFU). Please review the PI and IFU prior to using BLINCYTO®.

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.**

Please see additional Important Safety Information, including **BOXED WARNINGS,** on pages 36 and 37.

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

Amgen® Patient Navigator

A single point of contact to help answer questions about access and reimbursement, navigating treatment logistics, and to provide supplemental resources as your patients transition from hospital to outpatient care.

Amgen Patient Navigators can help with:

- Benefits verification and understanding coverage
- Prior authorization process
- Reimbursement and access resources

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.

Visit AmgenSupportPlus.com to learn how an Amgen Patient Navigator can help.

AMGEN Support+

Call (866) 264-2778 Monday through Friday, 9:00 AM to 8:00 PM ET or visit AmgenSupportPlus.com

Scan here to add Amgen® SupportPlus as a contact on your phone

AMGEN THERAPY LOCATOR™

Use this searchable database to locate standalone infusion centers, home infusion options, and outpatient options where BLINCYTO® may be able to be administered to your patients.*

Visit Amgen Therapy Locator™ at **AmgenTherapyLocator.com**

Find additional patient resources on www.BLINCYTO.com

*The information on this website is self-reported by independent third-party sites that administer treatment to patients or dispense product. It is not a comprehensive list of all sites that provide the therapies listed, and Amgen does not confirm the accuracy or otherwise endorse any of the sites on this list, which is subject to change. The information provided is not a guarantee of coverage, reimbursement, or availability of a product.

IMPORTANT SAFETY INFORMATION

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.

BLINCYTO® (blinatumomab) for injection
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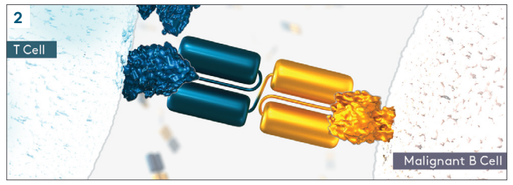
BLINCYTO® is a BiTE® therapy that binds CD3 and CD19[1]

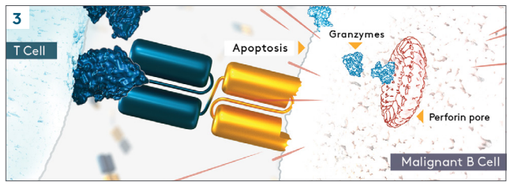
Target

BLINCYTO® targets malignant and benign B cells via the CD19 cell surface antigen while simultaneously engaging the patient's own T cells through the CD3 antigen.[2]



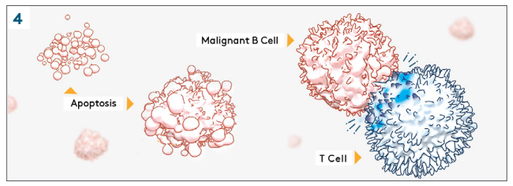
Activate

BLINCYTO® activates the T cell resulting in the formation of a synapse between the T cell and malignant B cell.[1]



Fight

The activated T cell then fights the malignant B cell by releasing perforin and granzymes through the perforin pore to induce apoptosis.[3]



Persist

The activated T cells persist in the blood stream, allowing for serial lysis of multiple target cells. Sustained activation of T cells results in local proliferation and enhanced polyclonal expansion of memory T cells, helping to fight cancer cells.[4]

BiTE, Bispecific T-cell Engager; CD, cluster of differentiation.

IMPORTANT SAFETY INFORMATION

- **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.

  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 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® and/or treat with corticosteroids as outlined in the PI. Advise outpatients to contact their healthcare professional if they develop signs or symptoms of neurological toxicities.

Please see additional Important Safety Information, including **BOXED WARNINGS**, on pages 36 and 37.

Starting BLINCYTO® treatment[1,5]

Administration[5]

- Administration of BLINCYTO® requires continuous intravenous (IV) infusion at a constant flow rate using an infusion pump that is programmable, lockable, non-elastomeric, and has an alarm

Inpatient scheduling for patients with B-cell precursor ALL[1]

- **Consolidation phase for Ph(–) disease:** Hospitalization is recommended for the first 3 days of the first cycle and the first 2 days of the second cycle
- **MRD(+):** Hospitalization is recommended for the first 3 days of the first cycle and the first 2 days of the second cycle
- **R/R:** Hospitalization is recommended for the first 9 days of the first cycle and the first 2 days of the second cycle
- For all subsequent cycle starts and reinitiations (eg, if treatment is interrupted for 4 or more hours), supervision by a healthcare professional or hospitalization is recommended

Discharge planning steps to consider

- Evaluate patient benefit coverage
- Confirm patient has an outside advocate (eg, family member or social worker)—include advocate in all care team discussions
- Establish multidisciplinary team (eg, nurse navigator, social worker, case manager)

Preparing for outpatient treatment considerations[1]

Confirm where your patient will continue BLINCYTO®

When not hospitalized, patients may potentially be treated with BLINCYTO® at one of the following locations. For these patients it may be helpful to consider the following:

Outpatient **clinic**

Infusion **center**

Home **infusion**

Outpatient clinic or infusion center

- Confirm availability of outpatient pharmacy and clinic service
- Assess patient's proximity to hospital or lodging near infusion facility and potential transportation needs
- Provide patient with clinic contact information
- Help patient understand/fill out patient postdischarge checklist

Home infusion

- Ensure medication can be stored correctly
- Verify where ambulatory infusion services are being provided
- Schedule a hospital introduction and first home visit by home healthcare provider; provide home health contact information

ALL, acute lymphoblastic leukemia; MRD, measurable or minimal residual disease; Ph(–), Philadelphia chromosome–negative; R/R, relapsed or refractory.

IMPORTANT SAFETY INFORMATION

- **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.

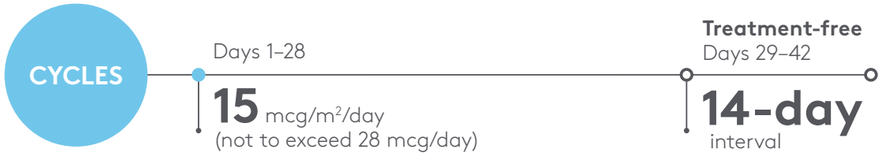
Please see additional Important Safety Information, including **BOXED WARNINGS**, on pages 36 and 37.

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

Consolidation phase for Ph(–) disease and MRD(+): BLINCYTO® dose and schedule[1]

Fixed dosing for patients weighing ≥ 45 kg[1]

BSA-based dosing for patients weighing < 45 kg



In the consolidation setting, a single cycle of BLINCYTO® monotherapy is 28 days of continuous intravenous (IV) infusion followed by a 14-day treatment-free interval (total 42 days)

- In the MRD(+) setting, a single cycle of treatment of BLINCYTO induction or consolidation consists of 28 days of continuous intravenous infusion followed by a 14-day treatment-free interval (total 42 days)
  - A treatment course consists of 1 cycle for induction followed by up to 3 additional cycles for consolidation

Special considerations[1]

- Hospitalization is recommended for the first 3 days of the first cycle and the first 2 days of the second cycle. For all subsequent cycle starts and reinitiation (eg, if treatment is interrupted for 4 or more hours), supervision by a healthcare professional or hospitalization is recommended
- Intrathecal chemotherapy prophylaxis is recommended before and during BLINCYTO® therapy to prevent central nervous system ALL relapse
- 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 (eg, ethanol, propylene glycol) which compete with benzyl alcohol for the same metabolic pathway. Serious adverse reactions, including fatal reactions and the "gasping syndrome," have been reported in very low birth weight neonates born weighing less than 1,500 g, and early preterm neonates who received intravenous drugs containing benzyl alcohol as a preservative

ALL, acute lymphoblastic leukemia; BSA, body surface area; IV, intravenous; Ph(–), Philadelphia chromosome–negative.

Premedication with dexamethasone[1]

	Consolidation phase for Ph(–) disease	MRD(+)
Adult patients	Premedicate with dexamethasone 20 mg intravenously within 1 hour prior to the first dose of each BLINCYTO® cycle	Premedicate with prednisone 100 mg intravenously or equivalent (eg, dexamethasone 16 mg) 1 hour prior to the first dose of each BLINCYTO® cycle
Pediatric patients	Premedicate with 5 mg/m² of dexamethasone intravenously or orally to a maximum dose of 20 mg prior to the first dose of BLINCYTO® in the first cycle and when restarting an infusion after an interruption of 4 or more hours in the first cycle	

IMPORTANT NOTE: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, BLINCYTO® should be infused through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration.[5]

It is very important that the instructions for preparation (including admixing) and administration provided in the Instructions for Use (IFU) are strictly followed to minimize medication errors (including underdose and overdose).[5]

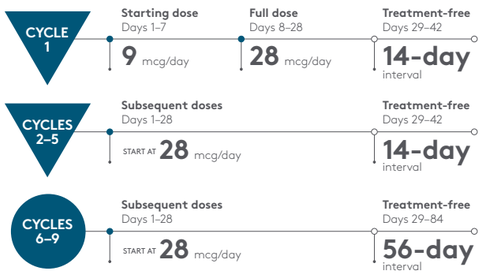
Discharge planning early on can be an important factor in a patient's smooth transition to outpatient treatment

MRD, measurable or minimal residual disease.

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

R/R: Patients may benefit from BLINCYTO® for up to 9 cycles[1]

Fixed dosing for patients weighing ≥ 45 kg



BSA-based dosing for patients weighing < 45 kg

A single cycle of treatment of BLINCYTO® induction or consolidation consists of 28 days of continuous intravenous infusion followed by a 14-day treatment-free interval (42 days total). A single cycle of treatment of BLINCYTO® continued therapy consists of 28 days of continuous intravenous infusion followed by a 56-day treatment-free interval (total 84 days).

- A treatment course consists of up to 2 cycles for induction followed by 3 additional cycles for consolidation (up to a total of 5 cycles)
- Continued therapy of up to 4 additional cycles may be given following consolidation treatment

Special considerations[1]

- Hospitalization is recommended for the first 9 days of the first cycle and the first 2 days of the second cycle. For all subsequent cycle starts and reinitiation (eg, if treatment is interrupted for 4 or more hours), supervision by a healthcare professional or hospitalization is recommended
- Intrathecal chemotherapy prophylaxis is recommended before and during BLINCYTO® therapy to prevent central nervous system ALL relapse
- 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 (eg, ethanol, propylene glycol) which compete with benzyl alcohol for the same metabolic pathway. Serious adverse reactions, including fatal reactions and the "gasping syndrome," have been reported in very low birth weight neonates born weighing less than 1,500 g, and early preterm neonates who received intravenous drugs containing benzyl alcohol as a preservative

Premedication with dexamethasone[1]

- For adult patients, premedicate with dexamethasone 20 mg intravenously or orally 1 hour prior to the first dose of BLINCYTO® of each cycle, prior to a step dose (such as cycle 1 day 8), and when restarting an infusion after an interruption of 4 or more hours
- For pediatric patients, premedicate with 5 mg/m^2 of dexamethasone intravenously or orally to a maximum dose of 20 mg prior to the first dose of BLINCYTO® in the first cycle, prior to a step dose (such as cycle 1 day 8), and when restarting an infusion after an interruption of 4 or more hours in the first cycle

ALL, acute lymphoblastic leukemia; BSA, body surface area; R/R, relapsed or refractory.

Please see additional Important Safety Information, including **BOXED WARNINGS**, on pages 36 and 37.

Flexible treatment plans that fit patient needs[1]

Administration[5]

Administration of BLINCYTO® requires a continuous intravenous (IV) infusion at a constant flow rate using an infusion pump that is programmable, lockable, non-elastomeric, and has an alarm.

Infusion duration and rate[5]

The final volume of infusion solution is more than the volume administered to the patient to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of BLINCYTO®.

- Infuse BLINCYTO® solution according to the instructions on the pharmacy label on the prepared bag at one of the following constant infusion rates:

24 hours	48 hours	72 hours*	96 hours*	7 days*
1 day	2 days	3 days	4 days	1 week
10 mL/hour for a duration of 24 hours	5 mL/hour for a duration of 48 hours	1.8 mL/hour for a duration of 72 hours	1.8 mL/hour for a duration of 96 hours	0.6 mL/hour for a duration of 7 days

At the end of the infusion, any unused BLINCYTO® solution in the IV bag and IV tubing should be disposed of in accordance with local requirements.

IMPORTANT NOTE: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, BLINCYTO® should be infused through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration.[5]

It is very important that the instructions for preparation (including admixing) and administration provided in the Instructions for Use (IFU) are strictly followed to minimize medication errors (including underdose and overdose).[5]

*Prepared with Bacteriostatic 0.9% Sodium Chloride Injection (containing 0.9% benzyl alcohol).[1]

Please see additional details in the full Prescribing Information (PI) and Instructions for Use (IFU) for BLINCYTO®.

IMPORTANT SAFETY INFORMATION

- **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.

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

Dosage modifications[1]

If the interruption after an adverse reaction is no longer than 7 days, continue the same cycle to a total of 28 days of infusion inclusive of days before and after the interruption in that cycle. If an interruption due to an adverse reaction is longer than 7 days, start a new cycle.

Adverse Reaction	Grade*	Patients weighing ≥ 45 kg	Patients weighing < 45 kg
Cytokine Release Syndrome (CRS)	Grade 3	**Interrupt** BLINCYTO®. **Administer** dexamethasone 8 mg every 8 hours intravenously or orally for up to 3 days, and taper thereafter over 4 days. When CRS is resolved, restart BLINCYTO® at 9 mcg/day, and escalate to 28 mcg/day after 7 days if the adverse reaction does not recur.	**Interrupt** BLINCYTO®. **Administer** dexamethasone 5 mg/m^2 (maximum 8 mg) every 8 hours intravenously or orally for up to 3 days, and taper thereafter over 4 days. When CRS is resolved, restart BLINCYTO® at 5 mcg/m^2/day, and escalate to 15 mcg/m^2/day after 7 days if the adverse reaction does not recur.
	Grade 4	**Discontinue** BLINCYTO® permanently. Administer dexamethasone as instructed for Grade 3 CRS.	
Neurological Toxicity†	Seizure	**Discontinue** BLINCYTO® permanently if more than one seizure occurs.	
	Grade 2 ICANS	**Interrupt** BLINCYTO® until ICANS resolves. Administer corticosteroids and manage according to current practice guidelines. When ICANS is resolved, restart BLINCYTO® at 9 mcg/day. Escalate to 28 mcg/day after 7 days if the adverse reaction does not recur.	**Interrupt** BLINCYTO® until ICANS resolves. Administer corticosteroids and manage according to current practice guidelines. When ICANS is resolved, restart BLINCYTO® at 5 mcg/m^2/day. Escalate to 15 mcg/m^2/day after 7 days if the adverse reaction does not recur.
	Grade 3 neurologic events including ICANS	**Withhold** BLINCYTO® until no more than Grade 1 (mild) and for at least 3 days, then restart BLINCYTO® at 9 mcg/day. Escalate to 28 mcg/day after 7 days if the adverse reaction does not recur. If the adverse reaction occurred at 9 mcg/day, or if the adverse reaction takes more than 7 days to resolve, discontinue BLINCYTO® permanently.	**Withhold** BLINCYTO® until no more than Grade 1 (mild) and for at least 3 days, then restart BLINCYTO® at 5 mcg/m^2/day. Escalate to 15 mcg/m^2/day after 7 days if the adverse reaction does not recur. If the adverse reaction occurred at 5 mcg/m^2/day, or if the adverse reaction takes more than 7 days to resolve, discontinue BLINCYTO® permanently.
		If ICANS, administer corticosteroids and manage according to current practice guidelines.	
	Grade 4 neurologic events including ICANS	**Discontinue** BLINCYTO® permanently. If ICANS, administer corticosteroids and manage according to current practice guidelines.	
Other Clinically Relevant Adverse Reactions	Grade 3	**Withhold** BLINCYTO® until no more than Grade 1 (mild), then restart BLINCYTO® at 9 mcg/day. Escalate to 28 mcg/day after 7 days if the adverse reaction does not recur. If the adverse reaction takes more than 14 days to resolve, discontinue BLINCYTO® permanently.	**Withhold** BLINCYTO® until no more than Grade 1 (mild), then restart BLINCYTO® at 5 mcg/m^2/day. Escalate to 15 mcg/m^2/day after 7 days if the adverse reaction does not recur. If the adverse reaction takes more than 14 days to resolve, discontinue BLINCYTO® permanently.
	Grade 4	**Consider discontinuing** BLINCYTO® permanently.	

*Based on the Common Terminology Criteria for Adverse Events (CTCAE). Grade 3 is severe, and Grade 4 is life-threatening.[1]
†Among patients that experienced a neurologic toxicity, the median time to the first event was within the first 2 weeks of BLINCYTO® treatment. The majority of neurologic toxicities resolved following interruption of BLINCYTO®, but some resulted in treatment discontinuation.[1]

ICANS, immune effector cell-associated neurotoxicity syndrome.

BLINCYTO® package contents and vials[1,5]

Each package of BLINCYTO® contains:[1]

One BLINCYTO® vial

- Supplied in a single-dose vial as a sterile, preservative-free, white to off-white lyophilized powder (35 mcg of BLINCYTO®/vial)

One IV solution stabilizer (IVSS) vial

- Supplied in a 10 mL single-dose glass vial as a sterile, preservative-free, colorless to slightly yellow, clear solution[1]
- The IVSS is injected into the IV bag prior to the addition of reconstituted BLINCYTO® to prevent adhesion of BLINCYTO® to the IV bags and IV tubing[5]
- **Do not use the IVSS to reconstitute BLINCYTO®[5]**

More than 1 package of BLINCYTO® may be needed to prepare some of the prescribed doses.[5]

Package and vials are not shown to scale

IMPORTANT NOTE: The package does not include preservative-free Sterile Water for Injection, USP, which should be used to reconstitute the lyophilized BLINCYTO® powder.[5] See pages 16–17 and 22–23 for a complete list of supplies needed that are not contained in the BLINCYTO® package.

IV, intravenous; USP, United States Pharmacopeia.

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

Storage and handling of BLINCYTO® and IVSS vials[1]

- Store BLINCYTO® and Intravenous Solution Stabilizer (IVSS) vials in the original package refrigerated at 2°C to 8°C (36°F to 46°F)
- BLINCYTO® and IVSS vials may be stored for a maximum of 8 hours at room temperature (23°C to 27°C [73°F to 81°F]) in the original carton to protect from light

Do not freeze.

Protect the vials of BLINCYTO® and IVSS from light until time of use.

Reconstituted BLINCYTO® and prepared infusion bags

The following table indicates the storage requirements for reconstituted BLINCYTO® vials and prepared BLINCYTO® infusion bags:

	Maximum storage time	
	Room temperature 23°C to 27°C (73°F to 81°F)	Refrigerated 2°C to 8°C (36°F to 46°F)
Reconstituted BLINCYTO® vial	4 hours	24 hours
Prepared BLINCYTO® 24-hour and 48-hour infusion bag (*Preservative-Free*)	48 hours*	8 days
Prepared BLINCYTO® 72-hour and 96-hour infusion bag *(with Preservative)*	4 days*	14 days
Prepared BLINCYTO® 7-day infusion bag (*with Preservative*)	7 days*	14 days

*Storage time includes infusion time. If the prepared BLINCYTO® infusion bag is not administered within the time frames and temperatures indicated, it must be discarded; it should not be refrigerated again.

What you need to know to prepare BLINCYTO®

Aseptic preparation and admixing area checklist[5]

Strictly observe aseptic technique when preparing the solution for infusion since BLINCYTO® vials do not contain antimicrobial preservatives. To prevent accidental contamination, prepare BLINCYTO® according to aseptic standards, including but not limited to:

- Prepare BLINCYTO® in a USP < 797 > compliant facility
- Prepare BLINCYTO® in an ISO Class 5 laminar flow hood or better
- Ensure that the admixing area has appropriate environmental specifications, confirmed by periodic monitoring
- Ensure that personnel are appropriately trained in aseptic manipulations and admixing of oncology drugs
- Ensure that personnel wear appropriate protective clothing and gloves
- Ensure that gloves and surfaces are disinfected

IMPORTANT NOTE: It is very important that the instructions for preparation (including admixing) and administration provided in the Instructions for Use (IFU) are strictly followed to minimize medication errors (including underdose and overdose).[5]

ISO, Organization for Standardization; USP, United States Pharmacopeia.

IMPORTANT SAFETY INFORMATION

- **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.

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

What you need to know about administration of BLINCYTO®[1]

Nursing considerations:

Verify before administering BLINCYTO®[1,5]

- The final volume in the prepared intravenous (IV) bag is greater than the volume that will be administered to the patient. Because of this overfill, IV bags may not completely empty during the infusion period[5]
- At the end of the infusion, any remaining BLINCYTO® solution in the IV bag and IV tubing should be disposed of in accordance with local requirements[5]
- The prepared IV bag can remain at room temperature for the amount of time noted below. If the prepared IV bag is not administered within the time frames and temperatures indicated, it must be discarded; it should not be refrigerated again[1]
  - **Prepared 24-hour and 48-hour infusion bags (preservative-free):** 48 hours*
  - **Prepared 72-hour and 96-hour infusion bags (with preservative):** 4 days*
  - **Prepared 7-day infusion bag (with preservative):** 7 days*
- The prepared IV bag can remain refrigerated for the following amount of time:[1]
  - **Prepared 24-hour and 48-hour infusion bags (preservative-free):** 8 days
  - **Prepared 72-hour and 96-hour infusion bags (with preservative):** 14 days
  - **Prepared 7-day infusion bag (with preservative):** 14 days

REMINDER: View infusion duration and rate information on page 9.

Additional information on the proper administration of BLINCYTO® can be found in the BLINCYTO® Prescribing Information and Instructions for Use and online at BLINCYTOHCP.com

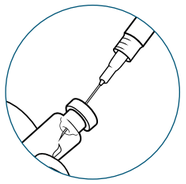
- The Amgen medical team can help answer questions regarding administration: 1-800-77-AMGEN (1-800-772-6436)

*Storage time includes infusion time. If the prepared BLINCYTO® infusion bag is not administered within the time frames and temperatures indicated, it must be discarded. Do not re-refrigerate.[1]

IMPORTANT SAFETY INFORMATION

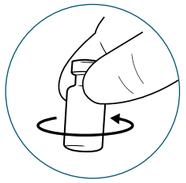
- **Elevated Liver Enzymes:** Transient elevations in liver enzymes have been associated with BLINCYTO® treatment with a median time to onset of 3 days. In patients receiving BLINCYTO®, although the majority of these events were observed in the setting of CRS, some cases of elevated liver enzymes were 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.

Reconstituting BLINCYTO® 24-hour, 48-hour, 72-hour, 96-hour, & 7-day infusion options[5]



STEP 1

- Determine the number of BLINCYTO® vials needed for a dose and infusion duration
- Reconstitute each BLINCYTO® vial with 3 mL of preservative-free Sterile Water for Injection, USP by directing the water along the walls of the BLINCYTO® vial and not directly on the lyophilized powder (resulting in a final BLINCYTO® concentration of 12.5 mcg/mL)
- **Do not** reconstitute BLINCYTO® with Intravenous Solution Stabilizer (IVSS)



STEP 2

Gently swirl the contents to avoid excess foaming. **Do not** shake.

STEP 3

Visually inspect the reconstituted solution for particulate matter and discoloration during reconstitution and prior to preparing the intravenous (IV) bag. The resulting solution should be clear to slightly opalescent, colorless to slightly yellow. **Do not** use if solution is cloudy or has precipitated.

USP, United States Pharmacopeia.

This guide does not take the place of the preparation and reconstitution instructions located in the Instructions for Use (IFU). Please review the IFU prior to using BLINCYTO®.

IMPORTANT SAFETY INFORMATION

- **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.

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

24- & 48-hour BLINCYTO® administration options[5]

This guide does not take the place of the preparation and reconstitution instructions located in the Instructions for Use (IFU). Please refer to the IFU for specific instructions to prepare BLINCYTO®.

In order to prepare BLINCYTO® solution for infusion for patients you will need to know:[1]

- The prescribed dose
- The infusion duration
- The patient's body surface area (BSA) for patients weighing < 45 kg

It is very important that the instructions for preparation (including admixing) and administration provided in the IFU are strictly followed to minimize medication errors (including underdose and overdose).[5]

Before preparation, ensure that you have the following supplies ready[5]

- **Weighing ≥ 45 kg:** 1 vial of BLINCYTO® is needed for preparation of 9 mcg/day dose or 28 mcg/day dose infused over 24 hours at a rate of 10 mL/hour
- **Weighing < 45 kg:** 1 vial of BLINCYTO® is needed for preparation of 5 mcg/m²/day or 15 mcg/m²/day dose infused over 24 hours at a rate of 10 mL/hour

- **Weighing ≥ 45 kg:** 1 vial of BLINCYTO® is needed for preparation of 9 mcg/day dose or 2 vials for preparation of 28 mcg/day dose infused over 48 hours at a rate of 5 mL/hour
- **Weighing < 45 kg:** 1 vial of BLINCYTO® is needed for preparation of 5 mcg/m²/day or 15 mcg/m²/day dose in patients with BSA ≤ 1.09 m^2, or 2 vials for 15 mcg/m²/day dose in patients with BSA > 1.09 m^2, infused over 48 hours at a rate of 5 mL/hour

Infusion duration and rate[5]

Infuse BLINCYTO® solution according to the instructions on the pharmacy label on the prepared bag at one of the following constant infusion rates

- Infusion rate of 10 mL/hour for a duration of 24 hours
- Infusion rate of 5 mL/hour for a duration of 48 hours

IMPORTANT SAFETY INFORMATION

- **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®.

 Please see additional Important Safety Information, including **BOXED WARNINGS**, on pages 36 and 37.

The following supplies are also required, but not included in the package:[5]

- Preservative-free Sterile Water for Injection, USP
- Preservative-free 0.9% Sodium Chloride Injection, USP
- Sterile, non-pyrogenic, low-protein-binding, 0.2 micron in-line filter
- Infusion bags/pump cassettes and intravenous tubing sets: Use either polyolefin, diethylhexylphthalate-free [DEHP-free] polyvinyl chloride [PVC], or ethyl vinyl acetate (EVA)

Special considerations for 24- or 48-hour BLINCYTO® infusion bags[5]

- Intravenous Solution Stabilizer (IVSS) is provided with the BLINCYTO® package and is used to coat the intravenous (IV) bag prior to addition of reconstituted BLINCYTO® to prevent adhesion of BLINCYTO® to IV bags and IV tubing. Therefore, add IVSS to the IV bag containing 0.9% Sodium Chloride Injection, USP. **Do not use IVSS for reconstitution of BLINCYTO®**
- The final volume of the admixed BLINCYTO® (270 mL) will be more than the volume administered to the patient (240 mL) to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of BLINCYTO®
- When preparing an IV bag, remove air from IV bag. This is particularly important for use with an ambulatory infusion pump
- Use the specific volumes described in the admixing instructions in the Instructions for Use (IFU) to minimize medication errors (including underdose and overdose)

USP, United States Pharmacopeia.

IMPORTANT SAFETY INFORMATION

- **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.

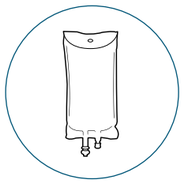
  Use the preservative-free preparations of BLINCYTO® where possible in neonates. When prescribing BLINCYTO® (with preservative) for neonatal patients, consider the combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative), other products containing benzyl 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® 72-Hour bag (with preservative) and 96-Hour bag (with preservative) contain 2.5 mg of benzyl alcohol per mL, and the 7-Day bag (with preservative) contains 7.4 mg of benzyl alcohol per mL.

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

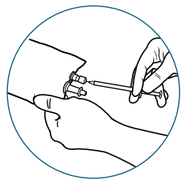
Preparation of the 24- & 48-hour BLINCYTO® infusion bags[5]

Verify the prescribed dose and infusion duration for each BLINCYTO® infusion bag. To minimize errors, **use the specific volumes described in the table on pages 20–21 to prepare the BLINCYTO® infusion bag.**



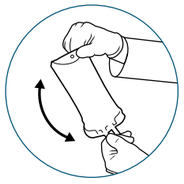
STEP 1

Aseptically add 270 mL of preservative-free 0.9% Sodium Chloride Injection, USP to the empty intravenous (IV) bag.



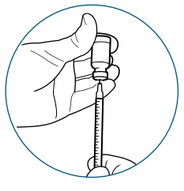
STEP 2

Aseptically transfer 5.5 mL of IV Solution Stabilizer (IVSS) to the IV bag containing preservative-free 0.9% Sodium Chloride Injection, USP.



- Gently mix the contents of the bag to avoid foaming. Discard the vial containing the unused IVSS

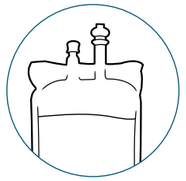
Reconstitution is required before step 3. See page 15 to learn how



STEP 3

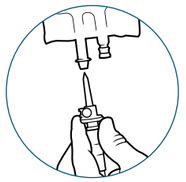
Aseptically transfer the required volume of reconstituted BLINCYTO® into the IV bag containing preservative-free 0.9% Sodium Chloride Injection, USP and IVSS.

- Use the tables on pages 20 and 21 to determine the specific volume of reconstituted BLINCYTO® required for the prescribed dose
- Gently mix the contents of the bag to avoid foaming
- Discard the vial containing unused BLINCYTO®



STEP 4

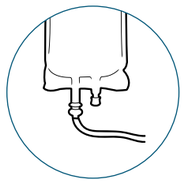
Remove air from the IV bag. This is particularly important for use with an ambulatory infusion pump.



STEP 5

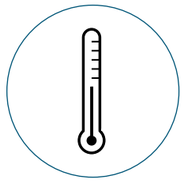
Under aseptic conditions, attach the IV tubing to the IV bag with the sterile 0.2 micron in-line filter.

- Ensure that the IV tubing is compatible with the infusion pump
- Use only polyolefin, diethylhexylphthalate-free [DEHP-free] polyvinyl chloride [PVC], or EVA IV tubing with a sterile, non-pyrogenic, low-protein-binding 0.2 micron in-line filter



STEP 6

Prime the IV tubing only with the solution in the bag containing the FINAL prepared BLINCYTO® solution for infusion.



STEP 7

Store refrigerated at 2°C to 8°C (36°F to 46°F) if not used immediately.

Additional storage directions and maximum storage times are listed on page 12.

IMPORTANT NOTE: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, BLINCYTO® should be infused through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration.

EVA, ethyl vinyl acetate; USP, United States Pharmacopeia.

Volumes to add to intravenous (IV) bag (by patient weight)[5]

For patients receiving a 24- or 48-hour infusion:

Preservative-free 0.9% Sodium Chloride injection, USP (starting volume)	270 mL
IV Solution Stabilizer (IVSS) (fixed volume for 24-hour and 48-hour infusion durations)	5.5 mL

For patients weighing ≥ 45 kg (fixed dose)

Infusion Duration	Dose	Infusion Rate	Reconstituted BLINCYTO®	
			Volume	Vials
24 hours	9 mcg/day	10 mL/hour	0.83 mL	1
	28 mcg/day	10 mL/hour	2.6 mL	1
48 hours	9 mcg/day	5 mL/hour	1.7 mL	1
	28 mcg/day	5 mL/hour	5.2 mL	2

IMPORTANT SAFETY INFORMATION

- **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.

For patients weighing < 45 kg (BSA-based dose)

Infusion Duration	Dose	Infusion Rate	BSA (m^2)	Reconstituted BLINCYTO®	
				Volume	Vials
24 hours	5 mcg/m^2/day	10 mL/hour	1.5–1.59	0.7 mL	1
			1.4–1.49	0.66 mL	1
			1.3–1.39	0.61 mL	1
			1.2–1.29	0.56 mL	1
			1.1–1.19	0.52 mL	1
			1–1.09	0.47 mL	1
			0.9–0.99	0.43 mL	1
			0.8–0.89	0.38 mL	1
			0.7–0.79	0.33 mL	1
			0.6–0.69	0.29 mL	1
			0.5–0.59	0.24 mL	1
			0.4–0.49	0.2 mL	1
			0.35–0.39	0.17 mL	1
			0.3–0.34	0.15 mL	1
			0.25–0.29	0.12 mL	1
			0.2–0.24	0.1 mL	1
24 hours	15 mcg/m^2/day	10 mL/hour	1.5–1.59	2.1 mL	1
			1.4–1.49	2 mL	1
			1.3–1.39	1.8 mL	1
			1.2–1.29	1.7 mL	1
			1.1–1.19	1.6 mL	1
			1–1.09	1.4 mL	1
			0.9–0.99	1.3 mL	1
			0.8–0.89	1.1 mL	1
			0.7–0.79	1 mL	1
			0.6–0.69	0.86 mL	1
			0.5–0.59	0.72 mL	1
			0.4–0.49	0.59 mL	1
			0.35–0.39	0.51 mL	1
			0.3–0.34	0.44 mL	1
			0.25–0.29	0.37 mL	1
			0.2–0.24	0.3 mL	1

For patients weighing < 45 kg (BSA-based dose)

Infusion Duration	Dose	Infusion Rate	BSA (m^2)	Reconstituted BLINCYTO®	
				Volume	Vials
48 hours	5 mcg/m^2/day	5 mL/hour	1.5–1.59	1.4 mL	1
			1.4–1.49	1.3 mL	1
			1.3–1.39	1.2 mL	1
			1.2–1.29	1.1 mL	1
			1.1–1.19	1 mL	1
			1–1.09	0.94 mL	1
			0.9–0.99	0.85 mL	1
			0.8–0.89	0.76 mL	1
			0.7–0.79	0.67 mL	1
			0.6–0.69	0.57 mL	1
			0.5–0.59	0.48 mL	1
			0.4–0.49	0.39 mL	1
			0.35–0.39	0.34 mL	1
			0.3–0.34	0.29 mL	1
			0.25–0.29	0.25 mL	1
			0.2–0.24	0.2 mL	1
48 hours	15 mcg/m^2/day	5 mL/hour	1.5–1.59	4.2 mL	2
			1.4–1.49	3.9 mL	2
			1.3–1.39	3.7 mL	2
			1.2–1.29	3.4 mL	2
			1.1–1.19	3.1 mL	2
			1–1.09	2.8 mL	1
			0.9–0.99	2.6 mL	1
			0.8–0.89	2.3 mL	1
			0.7–0.79	2 mL	1
			0.6–0.69	1.7 mL	1
			0.5–0.59	1.4 mL	1
			0.4–0.49	1.2 mL	1
			0.35–0.39	1 mL	1
			0.3–0.34	0.88 mL	1
			0.25–0.29	0.75 mL	1
			0.2–0.24	0.61 mL	1

For reconstitution instructions, please see page 15.

BSA, body surface area; USP, United States Pharmacopeia.

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

72-hour, 96-hour, & 7-day BLINCYTO® administration options[1,5]

This guide does not take the place of the preparation and reconstitution instructions located in the Instructions for Use (IFU). Please refer to the IFU for specific instructions to prepare BLINCYTO®.

In order to prepare BLINCYTO® solution for infusion for patients, you will need to know:[1]

- The prescribed dose
- The infusion duration
- The patient's body surface area (BSA) for patients weighing < 45 kg

It is very important that the instructions for preparation (including admixing) and administration provided in the full IFU are strictly followed to minimize medication errors (including underdose and overdose).[5]

Before preparation, ensure that you have the following supplies ready[5]

72 hours*
3 days

- **Weighing ≥ 45 kg:** 3 vials of BLINCYTO® are needed for preparation of 28 mcg/day dose infused over 72 hours at a rate of 1.8 mL/hour
- **Weighing < 45 kg:** 1 to 3 vials of BLINCYTO® are needed for preparation of 15 mcg/m^2/day dose infused over 72 hours at a rate of 1.8 mL/hour

96 hours*
4 days

- **Weighing ≥ 45 kg:** 4 vials of BLINCYTO® are needed for preparation of 28 mcg/day dose infused over 96 hours at a rate of 1.8 mL/hour
- **Weighing < 45 kg:** 1 to 3 vials of BLINCYTO® are needed for preparation of 15 mcg/m^2/day dose infused over 96 hours at a rate of 1.8 mL/hour

7 days*
1 week

- **Weighing ≥ 45 kg:** 6 vials of BLINCYTO® are needed for preparation of 28 mcg/day dose infused over 7 days at a rate of 0.6 mL/hour
- **Weighing < 45 kg:** 1 to 5 vials of BLINCYTO® are needed for preparation of 15 mcg/m^2/day dose infused over 7 days at a rate of 0.6 mL/hour

*Prepared with Bacteriostatic 0.9% Sodium Chloride Injection (containing 0.9% benzyl alcohol).[1]

The following supplies are also required, but not included in the package:[5]

- Preservative-free Sterile Water for Injection, USP
- Preservative-free 0.9% Sodium Chloride Injection, USP
- Bacteriostatic 0.9% Sodium Chloride Injection, USP
- Infusion bags/pump cassettes and intravenous tubing sets: Use either polyolefin, diethylhexylphthalate-free [DEHP-free] polyvinyl chloride [PVC], or ethyl vinyl acetate (EVA)†

†Do not use an in-line filter for 72-hour, 96-hour, or 7-day infusion bags.[5]

Special considerations for 72-hour, 96-hour, or 7-day infusion bags[5]

- Intravenous Solution Stabilizer (IVSS) is provided with the BLINCYTO® package and is used to coat the intravenous (IV) bag prior to addition of reconstituted BLINCYTO® to prevent adhesion of BLINCYTO® to IV bags and IV tubing. Therefore, add IVSS to the IV bag containing Bacteriostatic 0.9% Sodium Chloride Injection, USP. **Do not use IVSS for reconstitution of BLINCYTO®**
- The final volume of the admixed BLINCYTO® will be more than the volume administered to the patient to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of BLINCYTO®[5]
  - **72-hour infusion:** Final volume of 162 mL, volume administered 130 mL
  - **96-hour infusion:** Final volume of 200 mL, volume administered 173 mL
  - **7-day infusion:** Final volume of 110 mL, volume administered 100 mL
- When preparing an IV bag, remove air from IV bag. This is particularly important for use with an ambulatory infusion pump
- Use the specific volumes described in the admixing instructions in the IFU to minimize medication errors (including underdose and overdose)

Infusion duration and rate[5]

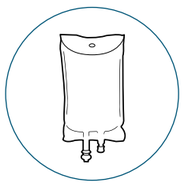
Infuse BLINCYTO® solution according to the instructions on the pharmacy label on the prepared bag at one of the following constant infusion rates

- Infusion rate of 1.8 mL/hour for a duration of 72 hours
- Infusion rate of 1.8 mL/hour for a duration of 96 hours
- Infusion rate of 0.6 mL/hour for a duration of 7 days

USP, United States Pharmacopeia.

Preparation of the 72-hour, 96-hour, & 7-day BLINCYTO® infusion bags[5]

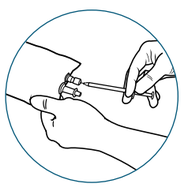
Verify the prescribed dose and infusion duration for each BLINCYTO® infusion bag. To minimize errors, **use the specific volumes described in the tables on pages 26–29 to prepare the BLINCYTO® infusion bag.**



STEP 1

Aseptically add the required volume of Bacteriostatic 0.9% Sodium Chloride Injection, USP to the empty intravenous (IV) bag.

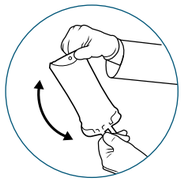
- **72-hour infusion:** 45 mL Bacteriostatic 0.9% Sodium Chloride Injection, USP
- **96-hour infusion:** 56 mL Bacteriostatic 0.9% Sodium Chloride Injection, USP
- **7-day infusion:** 90 mL Bacteriostatic 0.9% Sodium Chloride Injection, USP



STEP 2

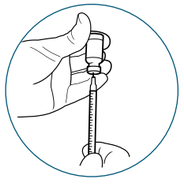
Aseptically transfer the required volume of IV Solution Stabilizer (IVSS) to the IV bag containing the Bacteriostatic 0.9% Sodium Chloride Injection, USP.

- **72-hour infusion:** 3.2 mL IVSS
- **96-hour infusion:** 4 mL IVSS
- **7-day infusion:** 2.2 mL IVSS



- Gently mix the contents of the bag to avoid foaming. Discard the vial containing the unused IVSS

Reconstitution is required before step 3. See page 15 to learn how

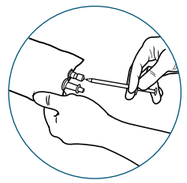


STEP 3

Aseptically transfer the required volume of reconstituted BLINCYTO® into the IV bag containing Bacteriostatic 0.9% Sodium Chloride Injection, USP and IVSS.

- Use the tables on pages 26–29 to determine the specific volume of reconstituted BLINCYTO® required for the prescribed dose
- Gently mix the contents of the bag to avoid foaming
- Discard the vial containing unused BLINCYTO®

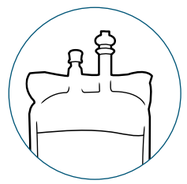
IMPORTANT NOTE: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, BLINCYTO® should be infused through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration.



STEP 4

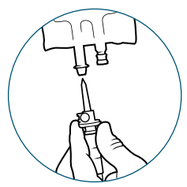
Aseptically transfer the needed volume of preservative-free 0.9% Sodium Chloride Injection, USP to the IV bag to obtain the required final volume.

- Use the tables on pages 26–29 to determine the specific volume of preservative-free 0.9% Sodium Chloride Injection, USP to obtain the required final volume
- Gently mix the contents of the bag to avoid foaming



STEP 5

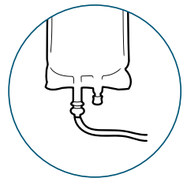
Remove air from the IV bag. This is particularly important for use with an ambulatory infusion pump.



STEP 6

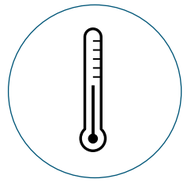
Under aseptic conditions, attach the IV tubing to the IV bag.

- Ensure that the IV tubing is compatible with the infusion pump
- Use only polyolefin, diethylhexylphthalate-free [DEHP-free] polyvinyl chloride [PVC], or ethyl vinyl acetate (EVA) IV tubing
- **Do NOT use an in-line filter for 72-hour, 96-hour, and 7-day bags**



STEP 7

Prime the IV tubing only with the solution in the bag containing the FINAL prepared BLINCYTO® solution for infusion.



STEP 8

Store refrigerated at 2°C to 8°C (36°F to 46°F) if not used immediately.

Additional storage directions and maximum storage times are listed on page 12.

USP, United States Pharmacopeia.

IMPORTANT SAFETY INFORMATION

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).

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

Volumes to add to intravenous (IV) bag (by patient weight)[5]

For patients between 5.4 kg and less than 45 kg receiving a 96-hour infusion:

Bacteriostatic 0.9% Sodium Chloride Injection, USP (starting volume)	• 72-hour infusion: 45 mL • 96-hour infusion: 56 mL • 7-day infusion: 90 mL
IV Solution Stabilizer (IVSS)	• 72-hour infusion: 3.2 mL • 96-hour infusion: 4 mL • 7-day infusion: 2.2 mL

For patients weighing ≥ 45 kg (fixed dose)

Infusion duration	Dose	Infusion rate	Reconstituted BLINCYTO®		Preservative-free 0.9% Sodium Chloride Injection, USP to qs to final volume*	Final volume of IV bag
			Volume	Vials		
72 hours	28 mcg/day	1.8 mL/hour	8.4 mL	3	105 mL	162 mL
96 hours	28 mcg/day	1.8 mL/hour	10.4 mL	4	130 mL	200 mL
7 days	28 mcg/day	0.6 mL/hour	16.8 mL	6	1 mL	110 mL

*Preservative-free 0.9% Sodium Chloride Injection, USP is added to quantity sufficient (qs) to the required final volume.

For patients between 5.4 kg and less than 45 kg receiving a 72-hour infusion:

For patients weighing ≥ 5.4 kg and < 45 kg (BSA-based dose)†

Infusion duration	Dose	Infusion rate	BSA (m^2)	Reconstituted BLINCYTO®		Preservative-free 0.9% Sodium Chloride Injection, USP to qs to final volume*	Final volume of IV bag
				Volume	Vials		
72 hours	15 mcg/m^2/day	1.8 mL/hour	1.5–1.59	6.8 mL	3	107 mL	162 mL
			1.4–1.49	6.4 mL	3	107 mL	162 mL
			1.30–1.39	6 mL	3	108 mL	162 mL
			1.20–1.29	5.4 mL	2	108 mL	162 mL
			1.10–1.19	5 mL	2	109 mL	162 mL
			1–1.09	4.6 mL	2	109 mL	162 mL
			0.9–0.99	4.2 mL	2	110 mL	162 mL
			0.8–0.89	3.8 mL	2	110 mL	162 mL
			0.7–0.79	3.2 mL	2	111 mL	162 mL
			0.6–0.69	2.8 mL	1	111 mL	162 mL
			0.5–0.59	2.3 mL	1	111 mL	162 mL
			0.4–0.49	2 mL	1	112 mL	162 mL
			0.35–0.39	1.7 mL	1	112 mL	162 mL
			0.3–0.34	1.4 mL	1	112 mL	162 mL
			0.25–0.29	1.2 mL	1	113 mL	162 mL

†The administration of BLINCYTO® as a 72-hour, 96-hour, and 7-day infusion is not recommended for patients weighing less than 5.4 kg.

BSA, body surface area; USP, United States Pharmacopeia.

Volumes to add to intravenous (IV) bag (by patient weight)[5]

For patients between 5.4 kg and less than 45 kg receiving a 96-hour infusion:

For patients weighing ≥ 5.4 kg and < 45 kg (BSA-based dose)*							
Infusion duration	Dose	Infusion rate	BSA (m^2)	Reconstituted BLINCYTO®		Preservative-free 0.9% Sodium Chloride Injection, USP to qs to final volume†	Final volume of IV bag
				Volume	Vials		
96 hours	15 mcg/m^2/day	1.8 mL/hour	1.5–1.59	8.4 mL	3	132 mL	200 mL
			1.4–1.49	7.8 mL	3	132 mL	200 mL
			1.30–1.39	7.4 mL	3	133 mL	200 mL
			1.20–1.29	6.8 mL	3	133 mL	200 mL
			1.10–1.19	6.2 mL	3	134 mL	200 mL
			1–1.09	5.6 mL	2	134 mL	200 mL
			0.9–0.99	5.2 mL	2	135 mL	200 mL
			0.8–0.89	4.6 mL	2	135 mL	200 mL
			0.7–0.79	4 mL	2	136 mL	200 mL
			0.6–0.69	3.4 mL	2	137 mL	200 mL
			0.5–0.59	2.8 mL	1	137 mL	200 mL
			0.4–0.49	2.4 mL	1	138 mL	200 mL
			0.35–0.39	2.1 mL	1	138 mL	200 mL
			0.3–0.34	1.8 mL	1	138 mL	200 mL
			0.25–0.29	1.5 mL	1	139 mL	200 mL

For patients between 5.4 kg and less than 45 kg receiving a 7-day infusion:

For patients weighing ≥ 5.4 kg and < 45 kg (BSA-based dose)*							
Infusion duration	Dose	Infusion rate	BSA (m^2)	Reconstituted BLINCYTO®		Preservative-free 0.9% Sodium Chloride Injection, USP to qs to final volume†	Final volume of IV bag
				Volume	Vials		
7 days	15 mcg/m^2/day	0.6 mL/hour	1.5–1.59	14 mL	5	3.8 mL	110 mL
			1.4–1.49	13.1 mL	5	4.7 mL	110 mL
			1.30–1.39	12.2 mL	5	5.6 mL	110 mL
			1.20–1.29	11.3 mL	5	6.5 mL	110 mL
			1.10–1.19	10.4 mL	4	7.4 mL	110 mL
			1–1.09	9.5 mL	4	8.3 mL	110 mL
			0.9–0.99	8.6 mL	4	9.2 mL	110 mL
			0.8–0.89	7.7 mL	3	10.1 mL	110 mL
			0.7–0.79	6.8 mL	3	11 mL	110 mL
			0.6–0.69	5.9 mL	3	11.9 mL	110 mL
			0.5–0.59	5 mL	2	12.8 mL	110 mL
			0.4–0.49	4.1 mL	2	13.7 mL	110 mL
			0.35–0.39	3.4 mL	2	14.4 mL	110 mL
			0.3–0.34	2.8 mL	1	15 mL	110 mL
			0.25–0.29	2.5 mL	1	15.3 mL	110 mL

*The administration of BLINCYTO® as a 72-hour, 96-hour, and 7-day infusion is not recommended for patients weighing less than 5.4 kg.
†Preservative-free 0.9% Sodium Chloride Injection, USP is added to quantity sufficient (qs) to the required final volume.

BSA, body surface area; USP, United States Pharmacopeia.

Administration of BLINCYTO® for 24-hour or 48-hour infusion[5]

- Administer BLINCYTO® as a continuous intravenous (IV) infusion at a constant flow rate using an infusion pump. The pump should be programmable, lockable, non-elastomeric, and have an alarm[5]
- The starting volume (270 mL) is more than the volume administered to the patient (240 mL) to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of BLINCYTO®[1]
- Infuse BLINCYTO® solution according to the instructions on the pharmacy label on the prepared bag at one of the following constant infusion rates:[5]
  - Infusion rate of 10 mL/hour for a duration of 24 hours, OR
  - Infusion rate of 5 mL/hour for a duration of 48 hours
- Administer the final prepared BLINCYTO® infusion solution using IV tubing that contains a sterile, non-pyrogenic, low-protein-binding, 0.2 micron in-line filter for 24-hour and 48-hour bags[5]
- **Important Note: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, infuse BLINCYTO® through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration[5]**
- At the end of the infusion, discard any unused BLINCYTO® solution in the IV bag and IV tubing in accordance with local requirements[5]

Administration of BLINCYTO® as a 72-hour, 96-hour, or 7-day infusion[5]

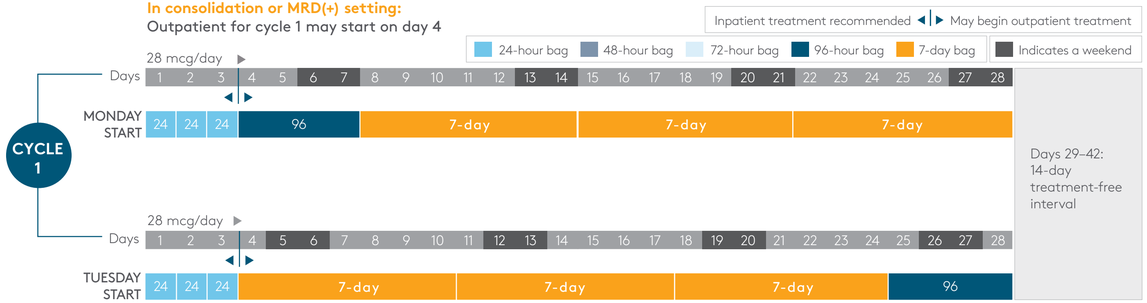
- Administer BLINCYTO® as a continuous IV infusion at a constant flow rate using an infusion pump. The pump should be programmable, lockable, non-elastomeric, and have an alarm[5]
- The final volume of infusion solution will be more than the volume administered to the patient to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of BLINCYTO®[5]
  - **72-hour infusion:** Final volume of 162 mL, volume administered 130 mL
  - **96-hour infusion:** Final volume of 200 mL, volume administered 173 mL
  - **7-day infusion:** Final volume of 110 mL, volume administered 100 mL
- **Do not use an in-line filter for 72-hour, 96-hour, or 7-day bags[5]**
- Infuse BLINCYTO® solution according to the instructions on the pharmacy label on the prepared bag at one of the following constant infusion rates:[5]
  - Infusion rate of 1.8 mL/hour for a duration of 72 hours or 96 hours, OR
  - Infusion rate of 0.6 mL/hour for a duration of 7 days
- **Important Note: Do not flush the BLINCYTO® infusion line, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof. When administering via a multi-lumen venous catheter, infuse BLINCYTO® through a dedicated lumen. Before flushing the catheter system, residual amounts of BLINCYTO® must be aspirated from the catheter system to avoid bolus administration[5]**
- At the end of the infusion, dispose of any unused BLINCYTO® solution in the IV bag and IV tubing in accordance with local requirements[5]

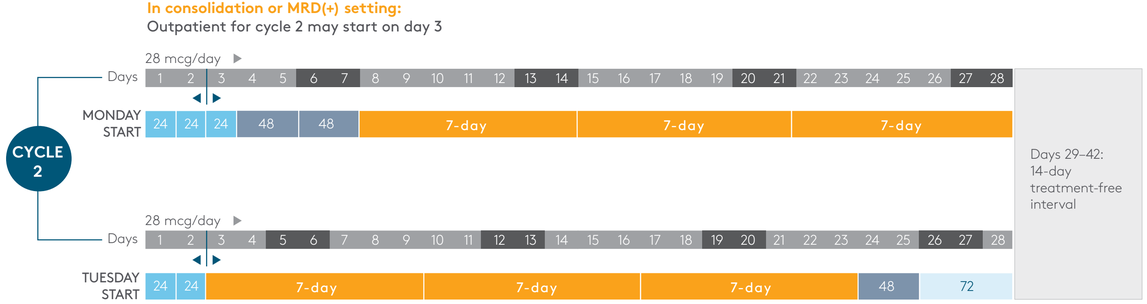
 Please see additional Important Safety Information, including **BOXED WARNINGS**, on pages 36 and 37.

Consolidation in Ph(–) and MRD(+) BCP-ALL: Flexible discharge infusion schedules[1]

Outpatient schedules start on different days depending on patient type*

Example infusion schedules for patients who are in consolidation or MRD(+) weighing ≥ 45 kg





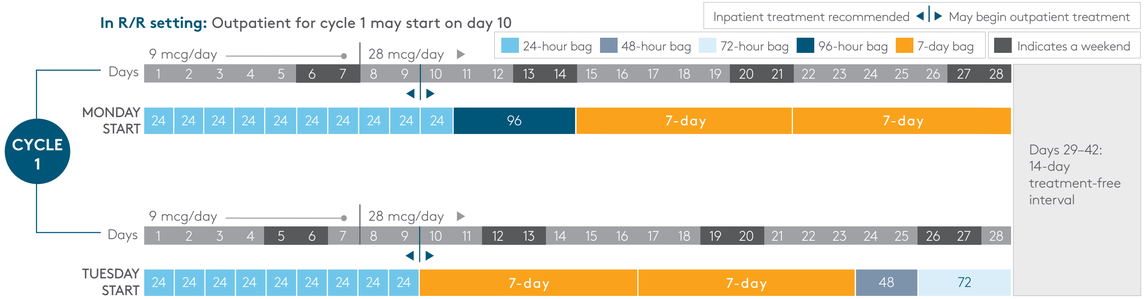
BCP-ALL, B-cell precursor acute lymphoblastic leukemia; MRD, measurable or minimal residual disease; Ph(–), Philadelphia chromosome-negative; R/R, relapsed or refractory.

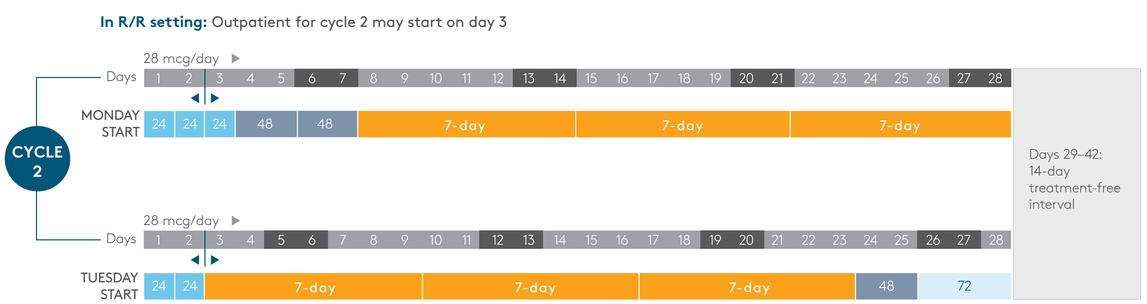
***Please see additional details in the full Prescribing Information for BLINCYTO®.**

R/R BCP-ALL: Flexible discharge infusion schedules[1]

Outpatient schedules start on different days depending on patient type*

Example infusion schedules for patients who are R/R weighing ≥ 45 kg





These infusion schedule examples are for illustrative purposes only, and may vary by patient and provider

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.
- **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.

  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 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® and/or treat with corticosteroids as outlined in the PI. Advise outpatients to contact their healthcare professional if they develop signs or symptoms of neurological toxicities.
- **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.
- **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® 72-Hour bag (with preservative) and 96-Hour bag (with preservative) contain 2.5 mg of benzyl alcohol per mL, and the 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).

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

Please see BLINCYTO® full Prescribing Information, including BOXED WARNINGS.

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

Amgen® Patient Navigator

A single point of contact to help answer questions about access and reimbursement, navigating treatment logistics, and to provide supplemental resources as your patients transition from hospital to outpatient care.

Amgen Patient Navigators can help with:

- Benefits verification and understanding coverage
- Prior authorization process
- Reimbursement and access resources

Visit AmgenSupportPlus.com to learn how an Amgen Patient Navigator can help.

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® Support+

Call (866) 264-2778 Monday through Friday, 9:00 AM to 8:00 PM ET or visit AmgenSupportPlus.com

Scan here to add Amgen® SupportPlus as a contact on your phone

Find additional patient resources on www.BLINCYTO.com

References: 1. BLINCYTO® (blinatumomab) prescribing information, Amgen. **2.** Yuraszeck T, Kasichayanula S, Benjamin J E. Translation and clinical development of bispecific T-cell engaging antibodies for cancer treatment. *Clin Pharmacol Ther.* 2017;101:634-645. **3.** Nagorsen D, Baeuerle PA. Immunomodulatory therapy of cancer with T cell-engaging BiTE antibody blinatumomab. *Exp Cell Res.* 2011;317:1255-1260. **4.** Baeuerle PA, Kufer P, Bargou R. BiTE: teaching antibodies to engage T-cells for cancer therapy. *Curr Opin Mol Ther.* 2009;11:22-30. **5.** BLINCYTO® (blinatumomab) instructions for use, Amgen.

Please see BLINCYTO® full Prescribing Information, including BOXED WARNINGS.

AMGEN

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