Up Close with Blinatumomab

This resource provides an overview of blinatumomab (BLINCYTO®).

Indications

Dosing & Administration

Cytokine Release Syndrome (CRS)

Neurotoxicity (including ICANS)

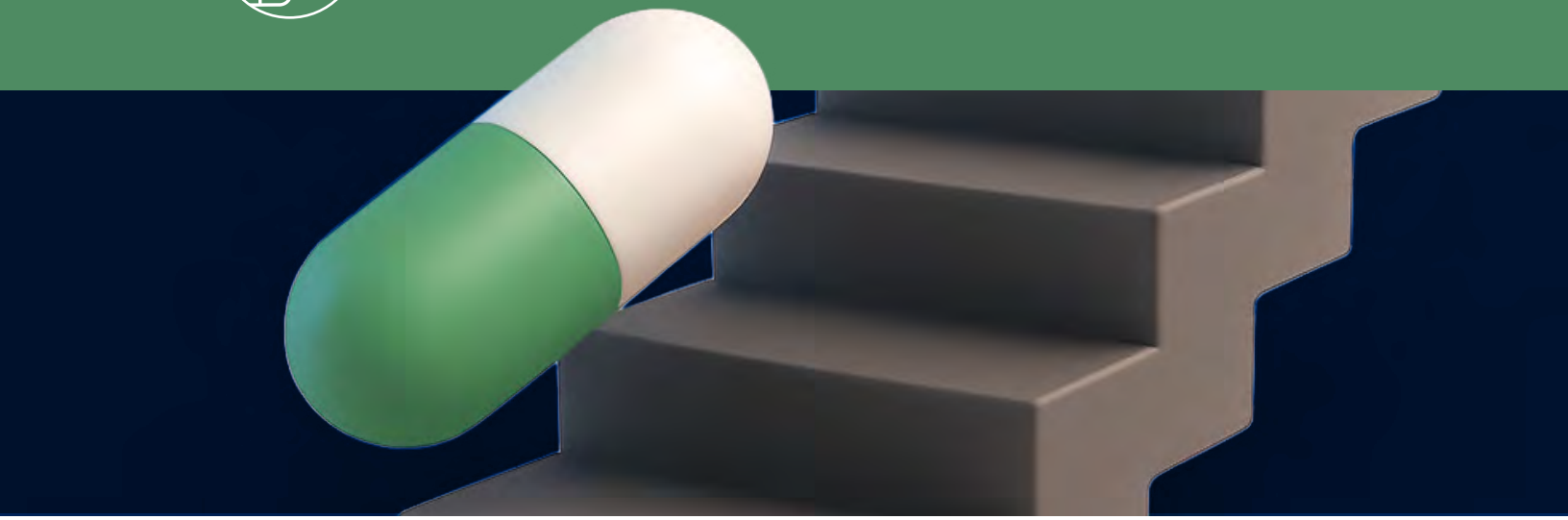
Other Toxicities

Indications

Blinatumomab is a **bispecific CD19-directed CD3 T cell engager** indicated for the treatment of adult and pediatric patients (aged 1 month or older) with:

- CD19-positive **B-cell precursor acute lymphoblastic leukemia (ALL)** in f**irst or second complete remission with measurable residual disease (MRD) ≥ 0.1%**
- **Relapsed or refractory** (R/R) CD19-positive B-cell precursor ALL
- CD19-positive **Philadelphia chromosome (Ph) B-cell precursor ALL** in the **consolidation phase of multiphase chemotherapy**

Dosing & Administration



Blinatumomab is administered as a **continuous intravenous (IV) infusion** at a constant flow rate using an infusion pump. Pre-medications and hospitalization requirements following administration are specific to the indication.

- Blinatumomab is recommended to be administered via a continuous IV infusion to adjust for its short half-life.

CD19-positive B-cell precursor ALL

A treatment course specific to this indication consists of 1 cycle of blinatumomab for induction followed by ≤ 3 cycles for consolidation.

- **Cycle length:** A single cycle (induction or consolidation) 28 days of continuous IV infusion followed by a 14-day treatment free interval (total 42 days).

Dosing Schedule	Day of Treatment[a]	Blinatumomab Dose[b,c] / Route	
		Patients Weighing ≥ 45 kg (fixed dose)	**Patients Weighing < 45 kg (BSA-based dose)**
Cycle 1 (Induction)	Days 1-28	20 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-42	14-day treatment free interval	
Cycle 2-4 (Consolidation)	Days 1-28	20 mcg/day IV	15 mcg/m^2/day IV Not to exceed 28 mcg/day
	Days 29-42	14-day treatment free interval	

Dosing Schedule	Day of Treatment[a]	Blinatumomab Dose[b,c] / Route

PO, orally; BSA, body surface area

[a]Hospitalization is recommended for the first 3 days of the first cycle and first 2 days of the second cycle. For all subsequent cycle starts and re-initiations, supervision by a healthcare professional or hospitalization is recommended.

[b]Intrathecal chemotherapy prophylaxis is recommended before and during blinatumomab therapy to prevent central nervous ALL relapse.

[c]All patients are to receive pre-medications as described below. Pre-medications should be completed 1 hour prior to the first dose in each cycle.

- **Adult patients:** premedicate with prednisone 100 mg IV (or equivalent such as dexamethasone 16 mg) prior to the first dose in each cycle
- **Pediatric patients:** premedicate with 5 mg/m^2 dexamethasone IV/PO (to a maximum for 20 mg) prior to the first dose in the first cycle and when restarting an infusion after a ≥ 4 hour interruption in the first cycle of all doses within the step-up dosing schedule

R/R CD19-positive B-cell precursor ALL

A treatment course specific to this indication consists of 2 induction cycles of blinatumomab followed by 3 additional cycles for consolidation, and up to 4 additional cycles of continued therapy (total 5 cycles, but up to 9).

- **Cycle length:** A single cycle of induction or consolidation consists of 28 days of continuous IV infusion followed by a 14-day treatment free interval (total 42 days). A single cycle of continued therapy consists of 28 days of continuous IV infusion followed by a 56-day treatment free interval (total 84 days).

Dosing Schedule	Day of Treatment[a]	Blinatumomab Dose[b,c] / Route	
		Patients Weighing ≥ 45 kg (fixed dose)	Patients Weighing < 45 kg (BSA-based dose)
Cycle 1 (Induction)	Days 1-7	9 mcg/day IV	5 mcg/m^2/day IV *Not to exceed 9 mcg/day*
	Days 8-28	28 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-42	14-day treatment free interval	
Cycle 2-4 (Induction)	Days 1-28	28 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-42	14-day treatment free interval	
Cycle 3-5 (Consolidation)	Days 1-28	28 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-42	14-day treatment free interval	
Cycle 6-9 (Continued Therapy)	Days 1-28	28 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-84	56-day treatment free interval	

Dosing Schedule	Day of Treatment[a]	Blinatumomab Dose[b,c] / Route

PO, orally; BSA, body surface area

[a]Hospitalization is recommended for the first 9 days of the first cycle and first 2 days of the second cycle. For all subsequent cycle starts and re-initiations, supervision by a healthcare professional or hospitalization is recommended.

[b]Intrathecal chemotherapy prophylaxis is recommended before and during blinatumomab therapy to prevent central nervous ALL relapse.

[c]All patients are to receive pre-medications as described below. Pre-medications should be completed 1 hour prior to the first dose in each cycle.

- **Adult patients:** premedicate with dexamethasone 20 mg IV/PO prior to the first dose of each cycle and when restarting an infusion after a ≥4 hours interruption in the first cycle
- **Pediatric patients:** premedicate with 5 mg/m^2 dexamethasone IV/PO (to a maximum for 20 mg) prior to the first dose in the first cycle, prior to a step-up dose (Cycle 1 Day 8) and when restarting an infusion after a ≥4 hour interruption in the first cycle

CD19-positive Ph B-cell precursor ALL in the consolidation phase of multiphase chemotherapy

A treatment course specific to this indication consists of 2 induction cycles of blinatumomab followed by 3 additional cycles for consolidation, and up to 4 additional cycles of continued therapy (total 5 cycles, but up to 9).

- **Cycle length:** A single cycle of induction or consolidation consists of 28 days of continuous IV infusion followed by a 14-day treatment free interval (total 42 days). A single cycle of continued therapy consists of 28 days of continuous IV infusion followed by a 56-day treatment free interval (total 84 days).

Dosing Schedule	Day of Treatment[a]	Blinatumomab Dose[b,c] / Route	
		Patients Weighing ≥ 45 kg (fixed dose)	Patients Weighing < 45 kg (BSA-based dose)
Consolidation Cycle	Days 1-28	28 mcg/day IV	15 mcg/m^2/day IV *Not to exceed 28 mcg/day*
	Days 29-42	14-day treatment free interval	

PO, orally; BSA, body surface area

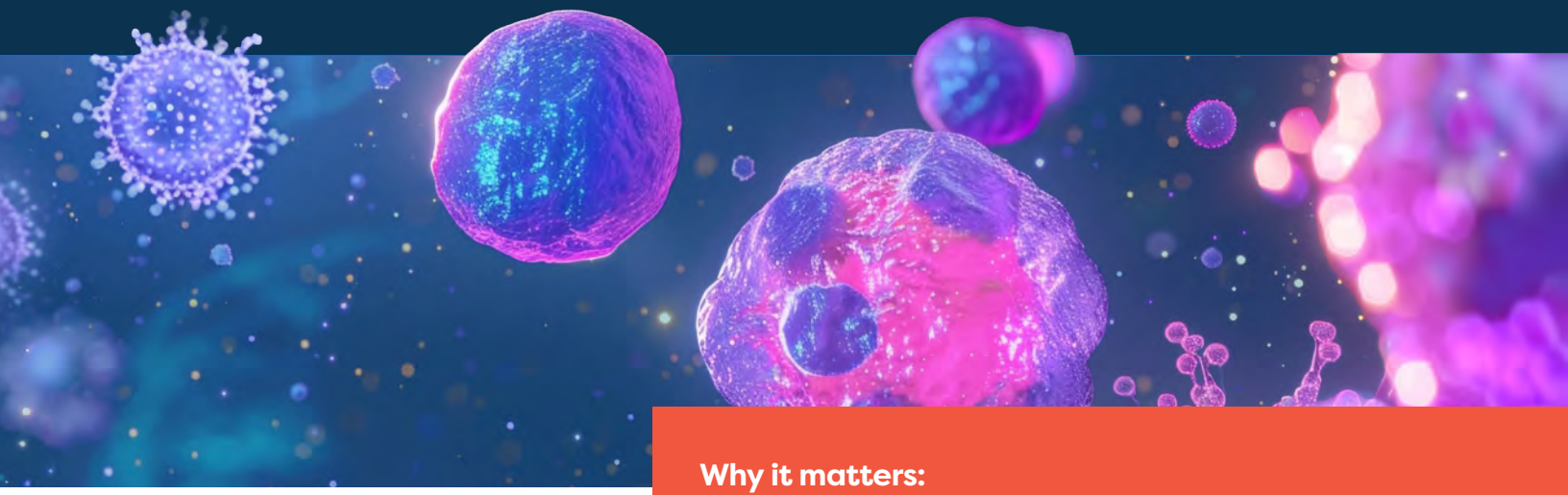
[a]Hospitalization is recommended for the first 9 days of the first cycle and first 2 days of the second cycle. For all subsequent cycle starts and re-initiations, supervision by a healthcare professional or hospitalization is recommended.

[b]Intrathecal chemotherapy prophylaxis is recommended before and during blinatumomab therapy to prevent central nervous ALL relapse.

[c]All patients are to receive pre-medications as described below. Pre-medications should be completed 1 hour prior to the first dose in each cycle.

- **Adult patients:** premedicate with dexamethasone 20 mg IV prior to the first dose of each cycle
- **Pediatric patients:** premedicate with 5 mg/m^2 dexamethasone IV/PO (to a maximum for 20 mg) prior to the first dose in the first cycle, prior to a step-up dose (Cycle 1 Day 8) and when restarting an infusion after a ≥4 hour interruption in the first cycle

Cytokine Release Syndrome



What is it? Cytokine release syndrome (CRS) is a systemic inflammatory response that can occur when the immune system is activated and releases large amounts of cytokines—proteins that help regulate immune responses.

Signs and symptoms:

- Chills
- Fever
- Low blood pressure
- Low tissue oxygen level
- Rapid heartbeat
- Trouble breathing

CRS is frequently graded using the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria.

Why it matters:

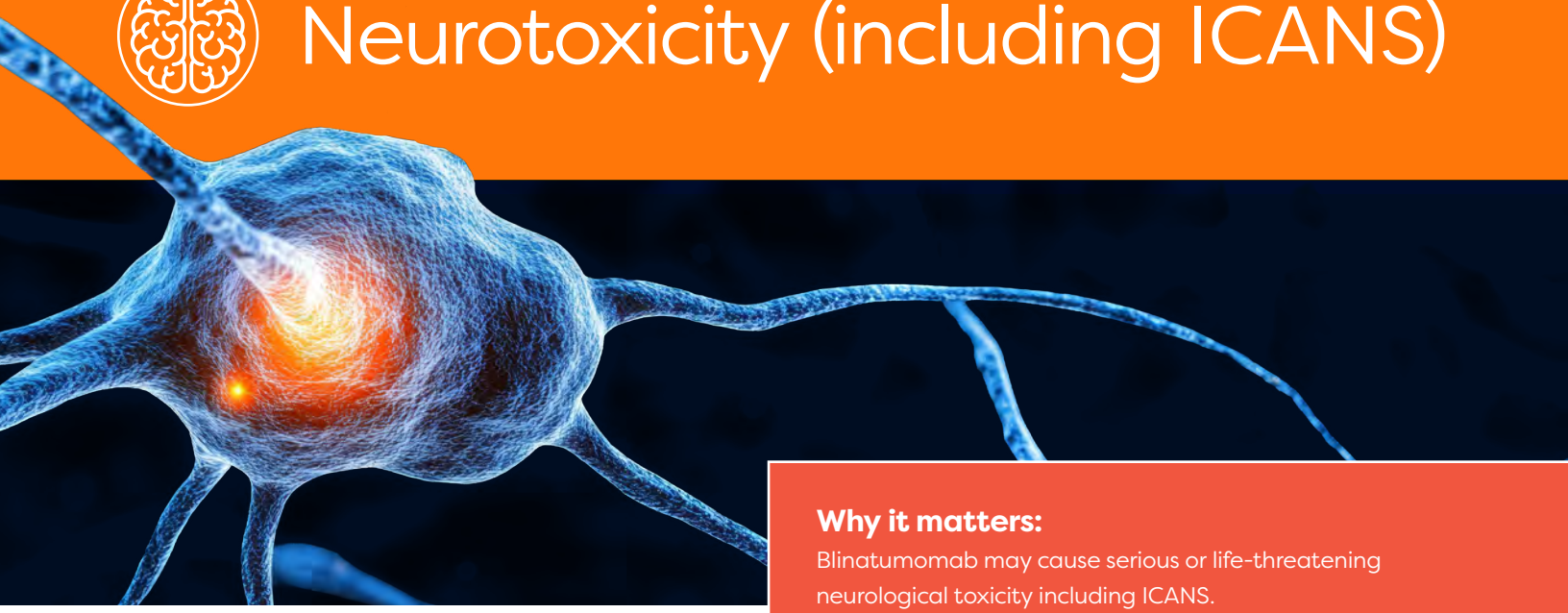
CRS occurred in patients who received blinatumomab during clinical trials. CRS was reported in **15%** of patients with R/R ALL, **7%** of patients with MRD-positive ALL, and in **16%** of patients who received blinatumomab in the consolidation phase of therapy.

- The median **time to onset** of CRS was **2 days** and **resolved** among most cases in **5 days**.
- Manifestations of CRS included: fever, nausea, hypotension, alanine amino transferase (ALT) or aspartate aminotransferase (AST), total bilirubin elevations, disseminated intravascular coagulations (DIC), headache, and asthenia.
  - **Some manifestations of CRS overlapped with infusion reactions** following completion of blinatumomab infusion. These manifestations included: capillary leak syndrome (CLS) and macrophage activation syndrome (MAS)/hemophagocytic lymphohystiocytosis (HLH).
- Care teams should monitor for signs/symptoms of these events.
  - Additionally, care teams should educate and advise patients receiving blinatumomab outpatient to contact their healthcare professional for any signs/symptoms of CRS.
  - If severe CRS occurs, treatment with blinatumomab should be withheld until CRS resolves.
    - Corticosteroids should be administered for severe or life-threatening CRS and blinatumomab should be discontinued permanently if these events occur.

THE BOTTOM LINE:

CRS occurred in patients across all clinical trials and may overlap with infusion-related reactions.

Neurotoxicity (including ICANS)



What is it? Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is characterized by various neurological symptoms resulting from the activation of the immune system and the resultant inflammatory processes.

Signs and symptoms:

- Confusion
- Dizziness
- Headache
- Memory issues
- Motor Deficits
- Shaking
- Trouble finding or words speaking

ICANS is frequently graded using the ASTCT consensus criteria.

THE BOTTOM LINE:

Neurologic problems are common with blinatumomab, however, ICANS is rare.

Why it matters:

Blinatumomab may cause serious or life-threatening neurological toxicity including ICANS.

- Across the three clinical trials the incidence of neurological toxicity was approximately **65%** and the incidence of **signs/symptoms consistent with ICANS criteria was 7.5%**.
- Neurological toxicity often had an **onset within the first 2 weeks** of blinatumomab treatment.
    - Manifestations of neurological toxicity varied by ages groups, however, were commonly presented as headache and tremor.
    - Approximately **13% of patients experienced Grade 3 or higher** neurological toxicity which resulted in convulsions, disturbances in consciousness, disorientation and confusion, encephalopathy, disorders in cranial nerve, speech, balance, and coordination.
- The onset of ICANS could be concurrent with CRS, following its resolution, or even in the absence of CRS.
- Care teams should monitor for signs/symptoms of neurological toxicity, including ICANS.
    - Additionally, care teams **should educate and advise patients receiving blinatumomab out-patient to contact their healthcare professional for any signs/symptoms of neurological toxicity. Patients should avoid driving or operating heavy machinery** while blinatumomab is being administered.
        - **Interruption or discontinuation** of blinatumomab may be recommended **depending on severity.**

Other Toxicities

Blinatumomab may cause other adverse reactions such as **infections, tumor lysis syndrome, elevated liver enzymes, neutropenia (including febrile neutropenia), leukoencephalopathy, benzyl alcohol toxicity (neonates only), and pancreatitis.**

Why it matters:
In addition to the risks of CRS and neurotoxicity (including ICANS), care teams need to be on the lookout for **other** blinatumomab-associated **toxicities**.

Infections. Blinatumomab may cause serious and fatal infections.

- Serious infections, including opportunistic infections, occurred in 25% of patients.
  - The most common serious infections reported were pneumonia, bacteremia, and sepsis.

THE BOTTOM LINE:

Care teams **should monitor patients for signs of infection before and during treatment**; treat appropriately.

- Additionally, care teams **should administer prophylactic antimicrobials and employ surveillance** testing during treatment.
  - **Avoid** administration of live vaccines **at least 2 weeks prior** to administration of blinatumomab, **throughout treatment, and until immune recovery**.
- **Based on severity,** blinatumomab **may need to be withheld or permanently discontinued**.

Neutropenia. Blinatumomab may cause neutropenia and febrile neutropenia as observed across all three clinical trials.

- In clinical trials, **decreased neutrophils** occurred in **62%** of patients, with **Grade 3 or 4** decreased neutrophils in **51%**.
  - **Febrile neutropenia** occurred in **2.2%** of patients.

THE BOTTOM LINE:

Care teams should monitor complete blood counts throughout treatment. Withhold or discontinue blinatumomab based on neutropenia severity.

Elevated Liver Enzymes. Blinatumomab may cause elevations in liver enzymes, including ALT or AST.

- In clinical trials, **liver enzyme elevations** initially occurred within the **3 days** and were associated with CRS. For events that occurred outside of CRS, the median time to onset was 19 days.
  - Some patients experienced **Grade 3 or higher** liver enzyme elevations **(7%) outside the setting of CRS** and lead to about **1% of discontinuation**.

THE BOTTOM LINE:

Care teams should **monitor liver enzymes routinely**, including AST/ALT/total bilirubin/gamma-glutamyl transferase (GGT), **prior to initiation** of blinatumomab and **during therapy**.

- **Hold blinatumomab** if the transaminases **rise to greater than 5 times the upper limit of normal or if total bilirubin rises to more than 3 times the upper limit of normal**.

Tumor Lysis Syndrome. Blinatumomab may cause a fatal or life-threatening condition, known as tumor lysis syndrome (TLS), as observed in the clinical trials. Tumor lysis syndrome is a condition that results from the rapid breakdown of tumor cells and the release of potassium, phosphate, calcium and uric acris into the bloodstream and can lead to widespread complications.

THE BOTTOM LINE:

Care teams should **provide appropriate prophylactic measures including pre-treatment nontoxic cytoreduction and on-treatment hydration** aimed for the prevention of TLS.

- Care teams should **consider temporary interruption or permanent discontinuation** of blinatumomab **depending on the severity**.

Pancreatitis. Post-marketing data has revealed that fatal pancreatitis has been reported in patients receiving blinatumomab concurrent with dexamethasone.

THE BOTTOM LINE:

Care teams should evaluate patients who develop any signs or symptoms of pancreatitis.

- Care teams should **consider temporary interruption or permanent discontinuation** of blinatumomab and dexamethasone **depending on the severity**.

Leukoencephalopathy. **Changes showing leukoencephalopathy** on cranial magnetic resonance imaging (MRI) have been observed in patients receiving blinatumomab, however at this time the **clinical significance of these changes is unknown**.

- These changes have especially been reported in patients who have received prior treatment with cranial irradiation and antileukemic chemotherapy, including intrathecal cytarabine or systemic high-dose methotrexate.

THE BOTTOM LINE:

Care teams should advise patients to receive routine follow-up including imaging as per institution-specific policies.

Benzyl Alcohol Toxicity (neonates only). Blinatumomab has been reported to cause very serious and fatal reactions (including gasping syndrome) in very-low birth weight (VLBW) neonates who were born weighing < 1500 g and early preterm neonates (born < 34 weeks gestational age) who received IV drugs containing the preservative, benzyl alcohol.

- VLBW neonates may be more likely to experience these adverse events due to a reduced ability to metabolize benzyl alcohol.

THE BOTTOM LINE:

Care teams should **use the preservative-free preparation of blinatumomab in neonates, when possible**.

- Prior to prescribing, care teams should consider the combined metabolic load of blinatumomab and other sources. The administration of blinatumomab via the 72-hour, 96-hour, and 7-day infusion is **not recommended in patients weighing < 5.4 kg**.
  - Additionally, care teams should monitor patients who receive the blinatumomab formulation that contains benzyl alcohol for any adverse reactions.

Embryo-Fetal Toxicity. Blinatumomab may cause fetal harm when administered to a pregnant woman.

- Advise **females of reproductive potential** to use effective contraception **during treatment** and for **at least 48 hours** after the last dose.
- Verify pregnancy status before initiating blinatumomab.

Use in Specific Populations

- **Lactation**: Advise women not to breastfeed during treatment and for 48 hours after the last dose.
- **Geriatric Use:** Of the total number of blinatumomab treated patients in these studies, 123 (8%) were 65 years of age and older and 21 (1%) were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients. Elderly patients did experience a higher rate of serious infections and neurological toxicities, including cognitive disorder, encephalopathy, and confusion.
- **Pediatric Use:** Safety and efficacy of blinatumomab has been studied in pediatric patients aged 1 month or older. The use of blinatumomab in patients < 1 month of age, has not yet been studied for any of the following indications referenced above.

References:

1. Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant.* 2019;25(4):625-638. doi:10.1016/j.bbmt.2018.12.758

2. BLINCYTO® (blinatumomab) [package insert]. Amgen Inc. Thousand Oaks, California. 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125557s032lbl.pdf

3. Locatelli F, Zugmaier G, Rizzari C, et al. Effect of blinatumomab vs chemotherapy on event-free survival among children with high-risk first-relapse b-cell acute lymphoblastic leukemia: a randomized clinical trial. *JAMA.* 2021;325(9):843-854. doi:10.1001/jama.2021.0987

4. Litzow MR, et al. Blinatumomab for MRD-negative acute lymphoblastic leukemia in adults. *N Engl J Med.* 2024;391(4):320-333. doi:10.1056/NEJMoa2312948

5. Kantarjian H, et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. *N Engl J Med.* 2017;376(9):836-847. doi:10.1056/NEJMoa1609783

6. Gökbuget N, Dombret H, Bonifacio M, et al. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia. *Blood.* 2018;131(14):1522-1531. doi:10.1182/blood-2017-08-798322

7. Martinelli G, Boissel N, Chevallier P, et al. Long-term follow-up of blinatumomab in patients with relapsed/refractory Philadelphia chromosome-positive B-cell precursor acute lymphoblastic leukaemia: final analysis of ALCANTARA study. *Eur J Cancer.* 2021;146:107-114. doi:10.1016/j.ejca.2020.12.022

8. von Stackelberg A, Locatelli F, Zugmaier G, et al. Phase I/phase II study of blinatumomab in pediatric patients with relapsed/refractory acute lymphoblastic leukemia. *J Clin Oncol.* 2016;34(36):4381-4389. doi:10.1200/JCO.2016.67.3301

9. Topp MS, Gökbuget N, Stein AS, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. *Lancet Oncol.* 2015;16(1):57-66. doi:10.1016/S1470-2045(14)71170-2