2018 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Blinatumomab (BLINCYTO®) recommended as a Category 1* treatment option for Ph(–) R/R B-cell precursor ALL.[1]

Intervene earlier—for all that's ahead

BLINCYTO® is the first and only immunotherapy to demonstrate superior OS vs chemotherapy in adult patients with Ph(–) R/R B-cell precursor ALL.[2-6,†]

TOWER landmark phase 3 study: BLINCYTO® single-agent immunotherapy was compared with chemotherapy in a large, international, prospective, randomized, phase 3 trial of 405 patients with Ph(–) relapsed/refractory B-cell precursor ALL.[2,5]

*National Comprehensive Cancer Network® (NCCN®) Categories of Evidence and Consensus; Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[1]

†The prespecified primary endpoint of OS was met in the landmark phase 3 TOWER study of BLINCYTO® vs chemotherapy.[5]

ALL, acute lymphoblastic leukemia; OS, overall survival; Ph(–), Philadelphia chromosome-negative; R/R, relapsed or refractory.

INDICATION

- BLINCYTO® is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

- **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, 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.

Click here to see full Prescribing Information, including **Boxed WARNINGS** and Medication Guide, for BLINCYTO®.

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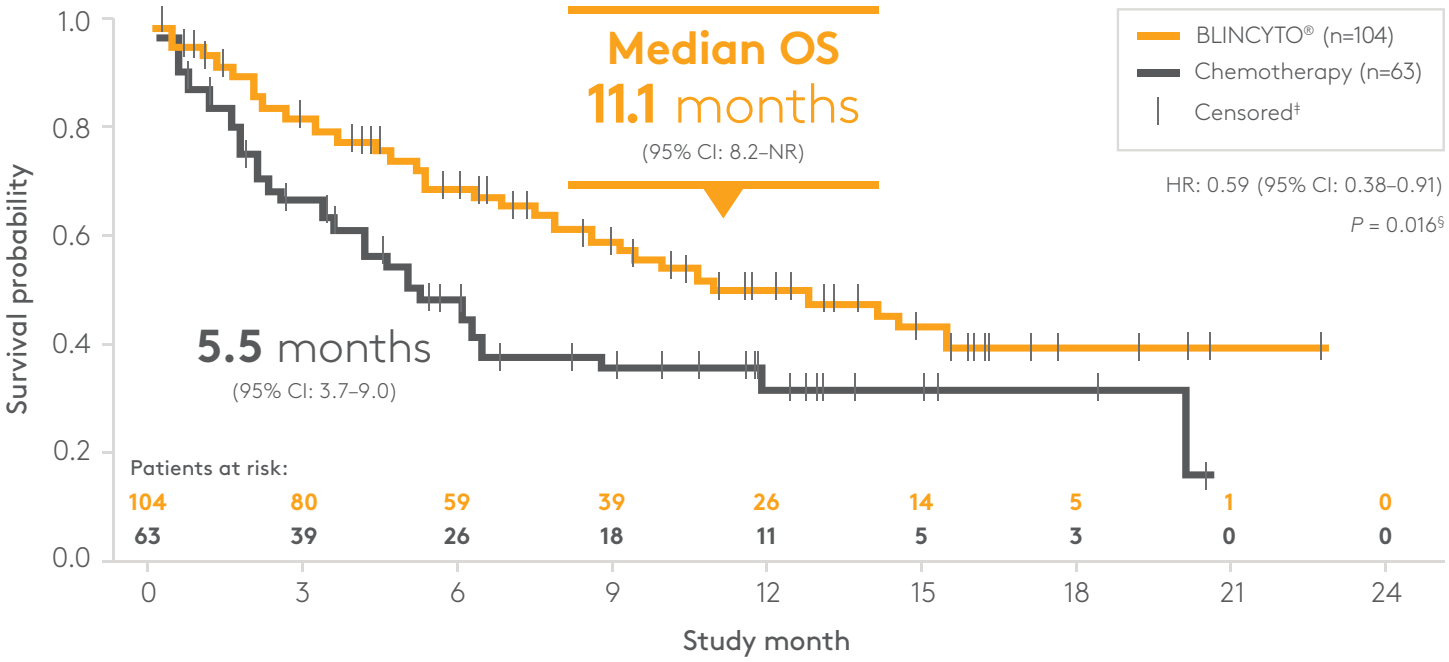
BLINCYTO® (blinatumomab) for injection
35 mcg single-dose vial

Intervening in first salvage with BLINCYTO® more than doubled median OS vs chemotherapy[7]

OS in patients treated in first salvage[7,†]



- BLINCYTO® demonstrated a greater median OS vs chemotherapy in the ITT population, 7.7 months (n=271) vs 4.0 months (n=134); *P* = 0.012; HR: 0.71 (95% CI: 0.55–0.93)[2,5]
- BLINCYTO® significantly increased complete remission rates compared with chemotherapy (CR/CRh*/CRi rates of 44% (119/271) vs 25% (33/134) for BLINCYTO® vs chemotherapy, respectively; *P* < 0.001)[5]

†OS in patients treated in first salvage was a prespecified subgroup analysis in TOWER; however, the OS efficacy in this subgroup was not a study objective, and the study was not powered to assess OS efficacy in this subgroup.[3]

‡A censored subject is indicated by a vertical bar.

§Stratified log-rank test.

CI, confidence interval; CR, complete remission; CRh*, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; HR, hazard ratio; ITT, intent-to-treat; NR, not reached; OS, overall survival.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Cytokine Release Syndrome (CRS): CRS, which may be life-threatening or fatal, occurred in 15% of patients with R/R ALL and in 7% of patients with MRD-positive ALL. 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 (TBILI), and disseminated intravascular coagulation (DIC). The manifestations of CRS after treatment with BLINCYTO® overlap with those of infusion reactions, capillary leak syndrome, and hemophagocytic histiocytosis/macrophage activation syndrome. 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.

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Choose BLINCYTO® for patients who do or do not proceed to HSCT

Deep and durable remission in patients treated with BLINCYTO®[5]

BLINCYTO® (n=119) vs chemotherapy (n=33)**

MRD(–) rates

76% vs 48%

Median DOR

7.3 vs 4.6 months

(95% CI: 5.8–9.9) vs (95% CI: 1.8–19.0)

Patients not proceeding to HSCT still achieved an OS benefit when treated with BLINCYTO®[5,††]

BLINCYTO® (n=271) vs chemotherapy (n=134)

Median OS

6.9 vs 3.9 months

HR: 0.66 (95% CI: 0.50–0.88)

In the TOWER study, treatment with BLINCYTO® resulted in no reports of treatment-related VOD, a life-threatening complication associated with HSCT[5,8,‡‡]

**Molecular remission[5] and DOR were assessed in patients achieving CR/CRh*/CRi, regardless of whether they proceeded to HSCT. MRD response was defined by PCR or flow cytometry ≤ 1 x 10^{-4}.

††OS in patients censored for allogeneic transplant was a prespecified sensitivity subgroup analysis in TOWER; however, the OS efficacy in this subgroup was not a study objective, and the study was not powered to assess OS efficacy in this subgroup.[3]

‡‡One patient treated with BLINCYTO® experienced fatal VOD in the TOWER trial but it was deemed non–treatment related by the investigator.[8]

DOR, duration of remission; HSCT, allogeneic hematopoietic stem cell transplantation; MRD, minimal residual disease; PCR, polymerase chain reaction; VOD, veno-occlusive disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

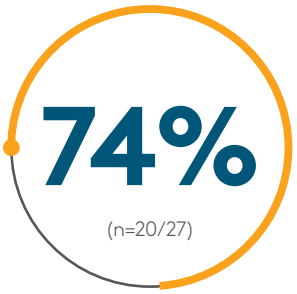
- Neurological Toxicities: Approximately 65% of patients receiving BLINCYTO® in clinical trials experienced neurological toxicities. The median time to the first event was within the first 2 weeks of BLINCYTO® treatment and the majority of events resolved. The most common (≥ 10%) manifestations of neurological toxicity were headache and tremor. Severe, life-threatening, or fatal 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. Monitor patients for signs or symptoms and interrupt or discontinue BLINCYTO® as outlined in the PI.

Please see additional Important Safety Information on Pages 10-11.

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

BLINCYTO® helped patients achieve and maintain a durable remission through up to 9 cycles[9]

27 patients in the landmark phase 3 TOWER study proceeded to continued therapy with BLINCYTO® after induction and consolidation



of patients **achieved a best response of complete remission** during continued therapy*

- Patients who received BLINCYTO® and had bone marrow blasts ≤ 5% after induction (up to 2 cycles) and consolidation (up to 3 cycles) with BLINCYTO® were eligible to receive continued therapy for an additional 12 months (4 weeks on treatment, 8 weeks off)[9]
- At the time of data collection for patients receiving continued therapy, 11 patients were continuing therapy with BLINCYTO®, while 16 had discontinued therapy due to: completion of maintenance therapy (n=3); intention to receive HSCT (n=4); intention to receive treatment other than HSCT (n=2); relapse (n=6); or an adverse event (n=1)[9]
- During continued therapy of cycles 6–9, no new safety concerns were identified; treatment-emergent adverse events included:[9]
  - 4 patients had a neurological event
  - 1 patient had CRS
- Overall safety event rates were lower in the continued therapy cycles versus the induction or consolidation cycles[9]

*CR was defined as ≤ 5% blasts in the bone marrow, no evidence of disease, and full recovery of peripheral blood counts (platelets > 100,000/microliter and ANC > 1,000/microliter).[2]

ANC, absolute neutrophil count; CR, complete remission; CRS, cytokine release syndrome; HSCT, allogeneic hematopoietic stem cell transplantation.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- 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.

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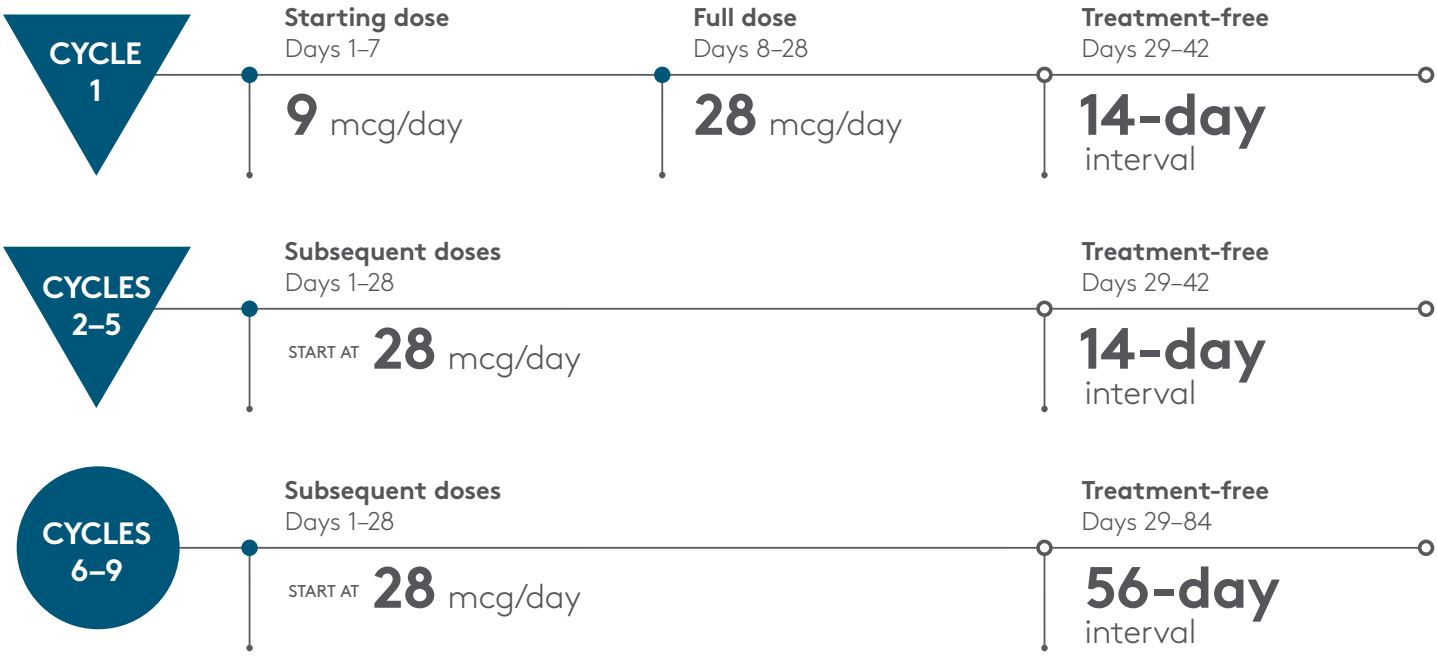
Dosing with BLINCYTO®[2]

Fixed dosing for patients weighing ≥ 45 kg[2]



- 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 (cycles 6–9) of up to 4 additional cycles may be given following consolidation treatment[2]
- A single cycle of induction or consolidation treatment consists of 28 days of continuous intravenous (cIV) infusion followed by a 14-day treatment-free interval (total 42 days)[2]
- A single cycle of continued therapy treatment consists of 28 days of cIV infusion followed by a 56-day treatment-free interval (total 84 days)[2]

For more flexible treatment options, BLINCYTO® can be infused over 24 hours, 48 hours, or 7 days[2,†]

†The 7-day infusion option uses bacteriostatic saline and is not recommended for patients weighing less than 22 kg.[2]

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

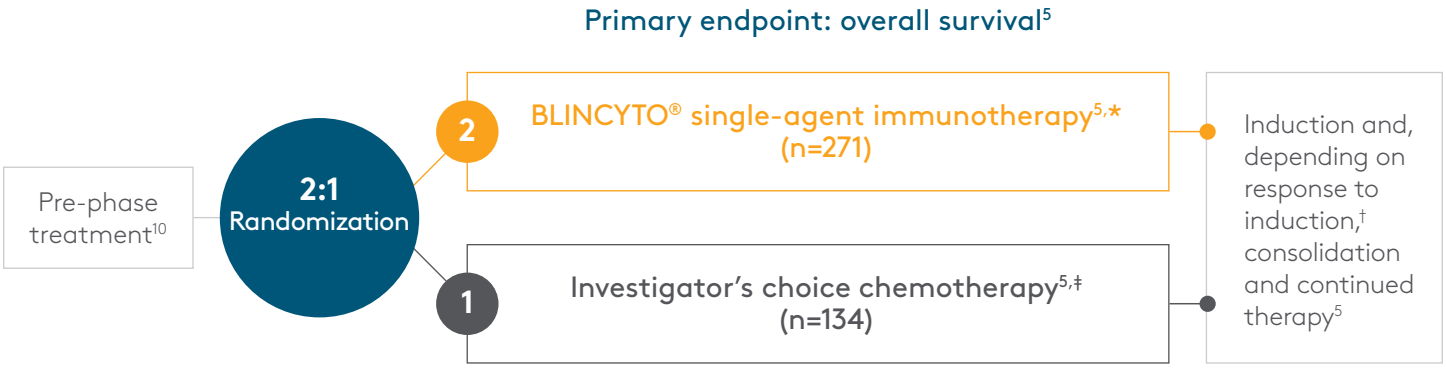
- Neutropenia and Febrile Neutropenia, including life-threatening cases, have been observed. Monitor appropriate laboratory parameters (including, but not limited to, white blood cell count and absolute neutrophil count) during BLINCYTO® infusion and interrupt BLINCYTO® if prolonged neutropenia occurs.
- Effects on Ability to Drive and Use Machines: Due to the possibility of neurological events, including seizures, 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.

Please see additional Important Safety Information on Pages 10-11.

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

The landmark phase 3 TOWER study

A phase 3 trial of 405 adult patients with Ph(–) R/R B-cell precursor ALL[5]



Pre-phase treatment

- All patients with > 50% BMB received dexamethasone (10 mg/m²/day up to a maximum of 24 mg/day) prior to randomization to reduce the risk of CRS associated with high tumor burden[10]
  - 14% (n=37/267) of patients treated with BLINCYTO® experienced CRS[2] of any grade, and 3% (n=8/267) experienced ≥ Grade 3

Premedication

- Patients treated with BLINCYTO® were premedicated[§] with 20 mg dexamethasone within 1 hour before infusion[2,10]

74% of patients on BLINCYTO® had a high tumor burden at baseline[5,]**

*Continuous IV infusion of 9 mcg/day on days 1–7 of cycle 1 and 28 mcg/day on remaining days of cycle 1 and for all subsequent cycles.[2]

†Patients achieving ≤ 5% BMB could continue with BLINCYTO® for consolidation (3 cycles of 4 weeks on, 2 weeks off) and continued therapy for an additional 12 months (4 weeks on, 8 weeks off).[5]

‡FLAG ± anthracycline–based regimen, HiDAC-based regimen, high-dose methotrexate–based regimen, or a clofarabine-based regimen.[5]

§Patients were premedicated prior to 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.[2,10]

**74% (n=201/271) of patients who received BLINCYTO® had a high tumor burden (≥ 50% BMB) at baseline.[5]

BMB, bone marrow blasts; CRS, cytokine release syndrome; FLAG, fludarabine, cytarabine, granulocyte colony-stimulating factor; HiDAC, high-dose cytarabine.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- 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 TBILI 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 TBILI rises to > 3 times ULN.

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BLINCYTO® was studied in a wide range of adult patients with R/R ALL, including those with a poor prognosis[2,5,11]

Baseline characteristics of the study population

	BLINCYTO® (n=271)	Chemotherapy (n=134)
Age		
Mean ± SD, years	41 ± 17	41 ± 17
Range, years	18–80	18–78
Study entry criteria, n (%)		
Refractory to primary or salvage therapy	115 (42)	54 (40)
In early first relapse (CR1 duration < 12 months)	**76 (28)**	**37 (28)**
In untreated second or later relapse††	32 (12)	16 (12)
Relapsed after allogeneic transplant††	46 (17)	27 (20)
Not specified	2 (1)	0 (0)
Prior salvage therapy, n (%)	171 (63)	70 (52)
Prior transplant, n (%)		
Yes	94 (35)	46 (34)
No	176 (65)	87 (65)
Disease burden, n (%)		
≥ 50% bone marrow blasts	**201 (74)**	**104 (78)**

- Patients in late first relapse (≥ 12 months after initial remission) were excluded

††Patients who met this study entry criterion met none of the above study entry criteria.

ALL, acute lymphoblastic leukemia; CR1, first complete remission; R/R, relapsed or refractory; SD, standard deviation.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- 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).

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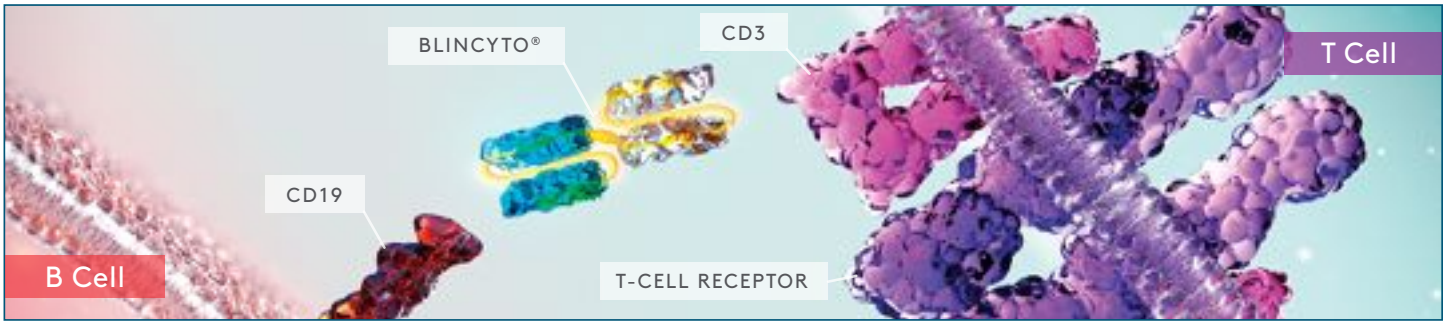
BLINCYTO® (blinatumomab) for injection
35 mcg single-dose vial

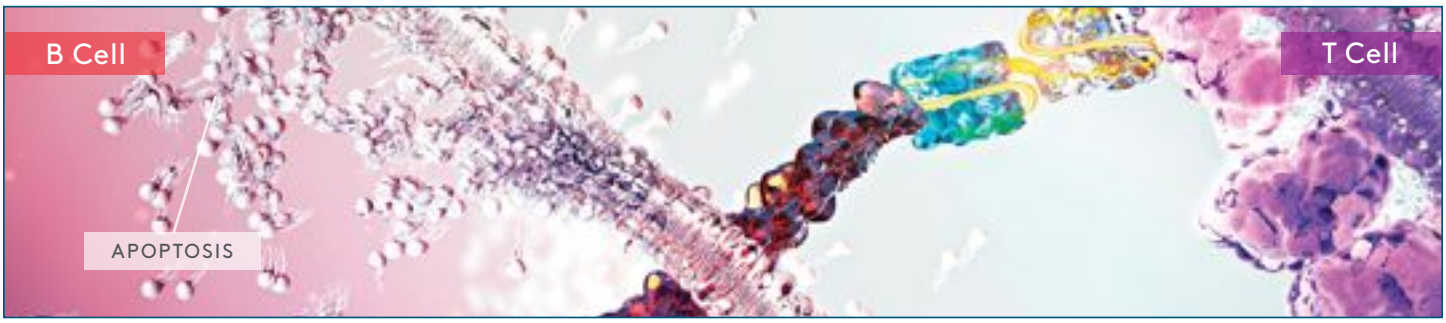
Engage the immune system with BLINCYTO®, a CD19-directed bispecific T cell engager[2]

Target BLINCYTO® activates endogenous T cells by connecting the CD3 antigen in the T-cell receptor complex with the CD19 surface antigen on benign and malignant B cells.[2]



Engage BLINCYTO® mediates the formation of a synapse between the T cell and the tumor cell, upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T cells.[2]

Activate Inflammatory cytokine release and T-cell proliferation result in redirected CD19+ cell lysis.[2]



CD, cluster of differentiation.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

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- **Neurological toxicities, which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® as recommended.**

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Lower rates of cytopenias and infections associated with BLINCYTO® vs chemotherapy[2]

Adverse reactions of any grade (≥ 20% incidence) or grade 3 or higher (≥ 5% incidence)[2] in cycle 1

Adverse reaction	BLINCYTO® (N=267)		Chemotherapy (N=109)	
	Any Grade* n (%)	≥ Grade 3* n (%)	Any Grade* n (%)	≥ Grade 3* n (%)
Blood and lymphatic system disorders				
Neutropenia[a]	84 (31)	76 (28)	67 (61)	61 (56)
Anemia[b]	68 (25)	52 (19)	45 (41)	37 (34)
Thrombocytopenia[c]	57 (21)	47 (18)	42 (39)	40 (37)
Leukopenia[d]	21 (8)	18 (7)	9 (8)	9 (8)
General disorders and administration-site conditions				
Pyrexia	147 (55)	15 (6)	43 (39)	4 (4)
Infections and infestations				
Infections — pathogen unspecified	74 (28)	40 (15)	50 (46)	35 (32)
Bacterial infectious disorders	38 (14)	19 (7)	35 (32)	21 (19)
Fungal infectious disorders	27 (10)	13 (5)	15 (14)	9 (8)
Injury, poisoning, and procedural complications				
Infusion-related reaction[e]	79 (30)	9 (3)	9 (8)	1 (1)
Investigations				
Hypertransaminasemia[f]	40 (15)	22 (8)	13 (12)	7 (6)
Nervous system disorders				
Headache	61 (23)	1 (< 1)	30 (28)	3 (3)

*Grading based on National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

[a]Neutropenia includes agranulocytosis, febrile neutropenia, neutropenia, and neutrophil count decreased.

[b]Anemia includes anemia and hemoglobin decreased.

[c]Thrombocytopenia includes platelet count decreased and thrombocytopenia.

[d]Leukopenia includes leukopenia and white blood cell count decreased.

[e]Infusion-related reaction is a composite term that includes the term infusion-related reaction and the following events occurring with the first 48 hours of infusion and the event lasted ≤ 2 days: pyrexia, cytokine release syndrome, hypotension, myalgia, acute kidney injury, hypertension, and rash erythematous.

[f]Hypertransaminasemia includes alanine aminotransferase increased, aspartate aminotransferase increased, hepatic enzyme increased, and transaminases increased.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- 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.

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35 mcg single-dose vial

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Contraindications

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Warnings and Precautions

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- 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, 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 TBILI 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 TBILI 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.

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- 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®.
- Risk of Serious Adverse Reactions in Pediatric Patients due to Benzyl Alcohol Preservative: Serious and fatal adverse reactions including "gasping syndrome," which is characterized by central nervous system depression, metabolic acidosis, and gasping respirations, can occur in neonates and infants treated with benzyl alcohol-preserved drugs including BLINCYTO® (with preservative). When prescribing BLINCYTO® (with preservative) for pediatric patients, consider the combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative) and other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known. Due to the addition of bacteriostatic saline, 7-day bags of BLINCYTO® solution for infusion with preservative contain benzyl alcohol and are not recommended for use in any patients weighing < 22 kg.

Adverse Reactions

- The most common adverse reactions (≥ 20%) in clinical trial experience of patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL (TOWER Study) treated with BLINCYTO® were infections (bacterial and pathogen unspecified), pyrexia, headache, infusion-related reactions, anemia, febrile neutropenia, thrombocytopenia, and neutropenia. Serious adverse reactions were reported in 62% of patients. The most common serious adverse reactions (≥ 2%) included febrile neutropenia, pyrexia, sepsis, pneumonia, overdose, septic shock, CRS, bacterial sepsis, device related infection, and bacteremia.
- Adverse reactions that were observed more frequently (≥ 10%) in the pediatric population compared to the adults with relapsed or refractory B-cell precursor ALL were pyrexia (80% vs. 61%), hypertension (26% vs. 8%), anemia (41% vs. 24%), infusion-related reaction (49% vs. 34%), thrombocytopenia (34% vs. 21%), leukopenia (24% vs. 11%), and weight increased (17% vs. 6%).
- In pediatric patients less than 2 years old (infants), the incidence of neurologic toxicities was not significantly different than for the other age groups, but its manifestations were different; the only event terms reported were agitation, headache, insomnia, somnolence, and irritability. Infants also had an increased incidence of hypokalemia (50%) compared to other pediatric age cohorts (15-20%) or adults (17%).

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).

INDICATION

- BLINCYTO® is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

References: 1. Referenced with permission from the NCCN 2018 Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.1.2018. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed November 14, 2018. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** BLINCYTO® (blinatumomab) prescribing information, Amgen. **3.** Data on file, Amgen; 2014. **4.** Data on file, Amgen; [1]; 2016. **5.** Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. *N Engl J Med*. 2017;376:836-847. **6.** Kantarjian H, DeAngelo DJ, Stelljes M, et al. Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia. *N Engl J Med*. 2016;375:740-753. **7.** Dombret H, Topp MS, Schuh A, et al. Blinatumomab vs SOC chemotherapy in first salvage compared with second or greater salvage in a phase 3 study. Presented at: 22nd Congress of the European Hematology Association; June 22-25, 2017; Madrid, Spain. Abstract S478. **8.** Data on file, Amgen; [2]; 2016. **9.** Rambaldi A, Huguet F, Zak P, et al. Maintenance therapy with blinatumomab in adults with relapsed/refractory B-precursor acute lymphoblastic leukemia: overall survival in adults enrolled in a phase 3 open-label trial. Presented at: 59th ASH Annual Meeting and Exposition; December 9–12, 2017; Atlanta, GA. Abstract 2552. **10.** Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. *N Engl J Med*. 2017;376:836-847. Supplementary Appendix; https://www.nejm.org/doi/suppl/10.1056/NEJMoa1609783/suppl_file/nejmoa1609783_appendix.pdf. Accessed November 14, 2018. **11.** Gökbuget N, Stanze D, Beck J, et al. Outcome of relapsed adult lymphoblastic leukemia depends on response to salvage chemotherapy, prognostic factors, and performance of stem cell transplantation. *Blood*. 2012;120:2032-2041.

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

Intervene earlier—for all that's ahead

BLINCYTO® vs chemotherapy

More than doubled median OS in first salvage[7,†]

11.1 months vs 5.5 months

BLINCYTO® (n=104) vs chemotherapy (n=63)

HR: 0.59 (95% CI: 0.38–0.91); *P* = 0.016[‡]

Deep and durable remission[5]

MRD(–) rates[§] were 76% vs 48%

BLINCYTO® (n=119) vs chemotherapy (n=33)

Median DOR[§] was 7.3 months vs 4.6 months

BLINCYTO® (n=119) vs chemotherapy (n=33)

(95% CI: 5.8–9.9) vs (95% CI: 1.8–19.0)

Greater median OS in patients not proceeding to HSCT[5,**]

6.9 months vs 3.9 months

BLINCYTO® (n=271) vs chemotherapy (n=134)

HR: 0.66 (95% CI: 0.50–0.88); *P* = 0.004

BLINCYTO® demonstrated a greater median OS vs chemotherapy in the ITT population, 7.7 months (n=271) vs 4.0 months (n=134); *P* = 0.012; HR: 0.71 (95% CI: 0.55–0.93).[2,5]

[†]OS in patients treated in first salvage was a prespecified subgroup analysis in TOWER; however, the OS efficacy in this subgroup was not a study objective, and the study was not powered to assess OS efficacy in this subgroup.[3]

[‡]Stratified log-rank test.

[§]Molecular remission[5] and DOR were assessed in patients achieving CR/CRh*/CRi. MRD response was defined by PCR or flow cytometry < 1 x 10^{-4}.

**OS in patients censored for allogeneic transplant was a prespecified sensitivity subgroup analysis in TOWER; however, the OS efficacy in this subgroup was not a study objective, and the study was not powered to assess OS efficacy in this subgroup.[3]

CI, confidence interval; CR, complete remission; CRh*, complete remission with partial hematologic recovery; CRi, complete remission with incomplete hematologic recovery; DOR, duration of remission; HR, hazard ratio; HSCT, allogeneic hematopoietic stem cell transplantation; ITT, intent-to-treat; MRD, minimal residual disease; OS, overall survival; PCR, polymerase chain reaction.

INDICATION

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IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

- **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, which may be severe, life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® as recommended.**

Click here to see full Prescribing Information, including **Boxed WARNINGS** and Medication Guide, for BLINCYTO®.

Please see additional Important Safety Information on Pages 10-11.

AMGEN®

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