UNDERSTANDING EXAMPLES OF

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

REIMBURSEMENT ACROSS SITES OF CARE

A BLINCYTO® patient transitions through multiple sites of care. This guide shows how major payers in the United States (commercial plans, Medicare, and Medicaid) offer coverage in each setting and reimburse for each component of care:

Drug

Pump and Supplies

Hospitalization

Professional Services (ie, drug administration)

INDICATIONS[1]

- BLINCYTO® (blinatumomab) is indicated for the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adult and pediatric patients.
- BLINCYTO® is indicated for the treatment of relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

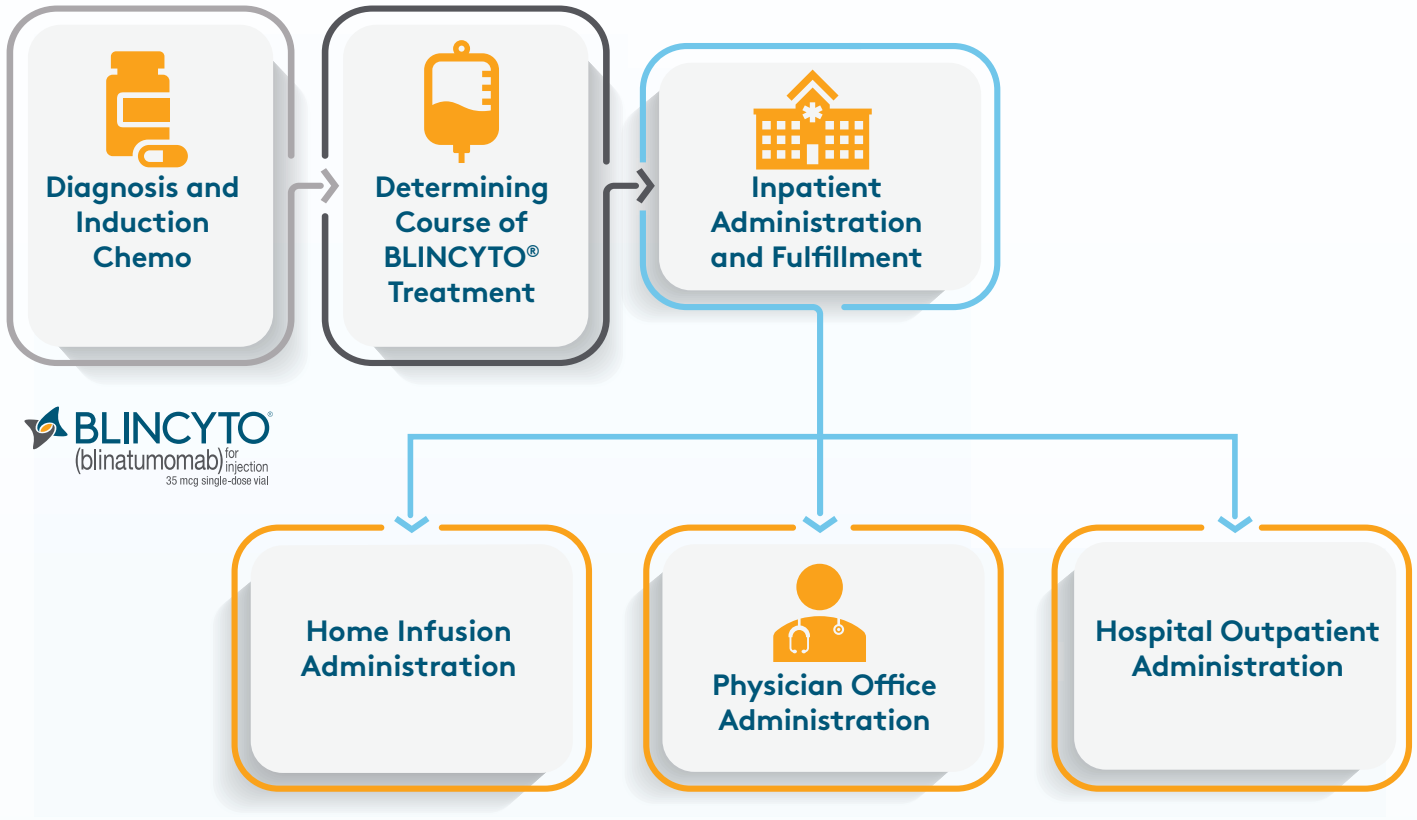
- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO®. Interrupt or discontinue BLINCYTO® and treat with corticosteroids as recommended.**
- **Neurological toxicities, which may be severe, life-threatening or fatal, occurred in patients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

Please see additional Important Safety Information on pages 5-6.

BLINCYTO® (blinatumomab) Reimbursement Process

Coverage of BLINCYTO® and its administration is required in all these sites of care to avoid interruption in treatment.

Patient Flow



The scenarios depicted above illustrate the most common ones for accessing BLINCYTO® via the buy-and-bill acquisition process, where the entity that acquires the product also administers it to the patient.

BLINCYTO® can also be acquired via a specialty pharmacy provider, including:

- Third-party specialty pharmacies that contract with a payer to supply specialty products covered under the medical benefit
- Specialty pharmacies owned by hospitals, physician offices, ambulatory infusion clinics, and/or home infusion companies that may also administer the medication

BLINCYTO® (blinatumomab)

Reimbursement Across Transitions in Site of Care

BLINCYTO®-eligible patients need coverage for the following: Drug + Pump + Hospitalization + Administration

Inpatient Hospital

Components of BLINCYTO® Care	Commercially Insured Patients	FFS Medicare Patients	FFS Medicaid Patients
BLINCYTO® **Pump and Supplies** **Hospitalization**	MS-DRG-based or global payment; typically includes BLINCYTO®[2] Reimbursement varies by contracts between providers and payers Some hospitals, in their contracts with managed care organizations, may negotiate a "carve out" benefit for drugs such as BLINCYTO® • May allow separate payment of such drugs outside of the bundled payment for inpatient services	MS-DRG payment includes BLINCYTO®[3] Covered under Medicare Part A benefit[4] Hospital may be eligible for outlier payments if cost of admission exceeds certain threshold Reimbursement varies for the 11 IPPS-Exempt Cancer Hospitals[5]	APR-DRG-based payment; typically includes BLINCYTO®[6] Reimbursement varies by state; may follow Medicare allowable amounts
Professional Services	Physician services may be covered separately outside of the bundled payment	Physician services may be covered and reimbursed according to the MPFS under Medicare Part B benefit	Physician services may be covered and paid outside of the bundled payment

Key: APR-DRG – All Patient-Refined Diagnosis Related Groups; FFS – fee-for-service; IPPS – Inpatient Prospective Payment System; MPFS – Medicare Physician Fee Schedule; MS-DRG – Medicare Severity Diagnosis-Related Group.

Outpatient Hospital

Components of BLINCYTO® Care	Commercially Insured Patients	FFS Medicare Patients	FFS Medicaid Patients
BLINCYTO®	Reimbursed based on contracted rates; methodology varies Examples[7]: • ASP + X% • WAC + X% • AWP – X% May need prior authorization	Covered under Medicare Part B benefit Typically reimbursed based on ASP + 6% when administered in a 340B hospital setting (with 2% sequestration reduction)[8,9] MUE cap of 210 units (approx. 6 vials) per date of service applies[10,11]	Reimbursement may be similar to Medicare OR State-defined limit (eg, California uses a federal upper limit)[12] May need prior authorization
Pump and Supplies	Reimbursement is bundled into the payment for the infusion service	Covered under Medicare Part B benefit Reimbursement is bundled into the payment for the infusion service	Reimbursed based on fee schedule or bundled into the payment for the infusion service Rates vary by state
Professional Services	Reimbursed based on contracted rate	Reimbursed based on the Medicare OPPS	

Key: ASP – average sales price; AWP – average wholesale price; FFS – fee-for-service; MUE – medically unlikely edit; OPPS – Outpatient Prospective Payment System; WAC – wholesale acquisition cost.
Note: The information here describes coverage and payment for BLINCYTO® under FFS Medicare and FFS Medicaid. Coverage and payment for patients enrolled in Medicare Advantage and/or Medicaid managed care organizations varies widely and is often similar to commercial insurance.

Physician Office

Components of BLINCYTO® Care	Commercially Insured Patients	FFS Medicare Patients	FFS Medicaid Patients
BLINCYTO®	Reimbursed based on contracted rates; methodology varies Examples[7]: • ASP + X% • WAC + X% • AWP – X% May need prior authorization	Covered under Medicare Part B benefit Typically reimbursed based on ASP + 6% (with 2% sequestration reduction)[9,13] MUE cap of 210 units (approx. 6 vials) per date of service applies[11,14]	Reimbursement may be similar to Medicare OR State-defined limit (eg, California uses a federal upper limit)[12] May need prior authorization
Pump and Supplies	Reimbursed based on contracted rate and bundled into payment for the infusion service	Covered under Medicare Part B benefit Reimbursement is bundled into the payment for the infusion service	Typically reimbursed based on fee schedule or bundled into the payment for the infusion service Rates vary by state
Professional Services	Reimbursed based on contracted rate	Reimbursed based on the MPFS	

Key: ASP – average sales price; AWP – average wholesale price; FFS – fee-for-service; MPFS – Medicare Physician Fee Schedule; MUE – medically unlikely edit; WAC – wholesale acquisition cost.

Home Infusion

Components of BLINCYTO® Care	Commercially Insured Patients	FFS Medicare Patients	FFS Medicaid Patients
BLINCYTO®	Reimbursed based on contracted rates; methodology varies Examples[7]: • ASP + X% • WAC + X% • AWP – X% May need prior authorization	Covered under Medicare Part B as long as it is supplied in a covered external infusion pump and the IV is initiated in home infusion setting[15] Typically reimbursed based on ASP + 6% (with 2% sequestration reduction)[9,13] Billing cap of 25 vials per month applies[16]	Reimbursement may be similar to Medicare OR State-defined limit (eg, California uses a federal upper limit)[19] May need prior authorization
Pump and Supplies	Reimbursed based on contracted rate	Covered under Medicare Part B benefit Reimbursed as part of the Medicare DMEPOS Fee Schedule[17]	Typically reimbursed based on fee schedule Rates vary by state
Professional Services	Reimbursed based on contracted rate	Covered under Part B Reimbursed under the home infusion therapy services benefit in 15-minute increments for applicable providers[18]	

Key: ASP – average sales price; AWP – average wholesale price; DMEPOS – Durable Medical Equipment Prosthetics, Orthotics, and Supplies; FFS – fee-for-service; WAC – wholesale acquisition cost.
Note: Medicare home infusion benefit is distinct and separate from the Medicare home health benefit.

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

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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.**

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 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.
- 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.
- 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, 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.
- 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).

Please see additional Important Safety Information on the next page.

IMPORTANT SAFETY INFORMATION (CONTINUED)

- Immunization: Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to the start of BLINCYTO® treatment, during treatment, and until immune recovery following last cycle of BLINCYTO®.
- Benzyl Alcohol Toxicity in Neonates: Serious adverse reactions, including fatal reactions and the "gasping syndrome," have been reported in very low birth weight (VLBW) neonates born weighing less than 1500 g, and early preterm neonates (infants born less than 34 weeks gestational age) who received intravenous drugs containing benzyl alcohol as a preservative. Early preterm VLBW neonates may be more likely to develop these reactions, because they may be less able to metabolize benzyl alcohol.
  Use the preservative-free preparations of BLINCYTO® where possible in neonates. When prescribing BLINCYTO® (with preservative) for neonatal patients, consider the combined daily metabolic load of benzyl alcohol from all sources including BLINCYTO® (with preservative), other products containing benzyl alcohol or other excipients (e.g., ethanol, propylene glycol) which compete with benzyl alcohol for the same metabolic pathway.
  Monitor neonatal patients receiving BLINCYTO® (with preservative) for new or worsening metabolic acidosis. The minimum amount of benzyl alcohol at which serious adverse reactions may occur in neonates is not known. The BLINCYTO® 7-Day bag (with preservative) contains 7.4 mg of benzyl alcohol per mL
- Embryo-Fetal Toxicity: Based on its mechanism of action, BLINCYTO® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with BLINCYTO® and for 48 hours after the last dose.

Adverse Reactions

- The most common adverse reactions (≥ 20%) are pyrexia, infusion-related reactions, infections (pathogen unspecified), headache, neutropenia, anemia, and thrombocytopenia.

Dosage and Administration Guidelines

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

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

REFERENCES

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