Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Blinatumomab (Blincyto®)	MP-RX-FP-14-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Blincyto® (blinatumomab), a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of certain patients with CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) and CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia (ALL).

Background Information

Blyncito is a bispecific T-cell engager designed to promote lysis of cancer cells by binding simultaneously with both CD3 on cytotoxic T-cells and CD19 on certain cancerous B-cells. It is used to treat acute lymphoblastic leukemia (ALL). Blincyto should only be used in CD19+ B-cell ALL due to its molecular target.

The FDA-approved indications for BLINCYTO include the treatment of CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients one month and older who are in first or second complete remission with minimal residual disease (MRD) ≥ 0.1%, or who have relapsed or refractory ALL. Additionally, it is approved for the treatment of CD19-positive Philadelphia chromosome-negative B-cell precursor ALL in the consolidation phase of multiphase chemotherapy. NCCN also recommends Blincyto in combination with various other chemotherapy regimens, as consolidation therapy, and as maintenance therapy alternating with POMP (prednisone, vincristine, methotrexate, and mercaptopurine). NCCN guidelines for Pediatric Acute Lymphoblastic Leukemia also recommend the use of Blincyto in combination with Interfant regimens for patients with KMT2A (11q23) rearrangement status. KMT2A rearrangement is a genetic marker associated with high-risk leukemia in infants, which affects the treatment plan, often requiring more aggressive therapy like Interfant regimens. Interfant regimens involve intensive multi-agent chemotherapy, CNS prophylaxis, and, in some cases, stem cell transplantation specifically designed for infants diagnosed with ALL and are described in further detail within the guidelines.

Blincyto has a black box warning for cytokine release syndrome (CRS). If severe CRS occurs, Blincyto should be interrupted until resolution, or permanently discontinued if life-threatening CRS. Blincyto also has a black box warning for neurological toxicities. There is limited experience in patients with active ALL in the central nervous system (CNS) or a history of neurologic events as patients with clinically relevant CNS pathology were excluded from studies.

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Definitions and Measures

- Complete Response or Complete Remission (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.
    - First Complete Remission (CR): The patient has responded well to initial treatment, with no signs or symptoms of leukemia based on specific criteria.
    - Second Complete Remission (CR): Occurs after a relapse and subsequent treatment.
- Consolidation Therapy: phase of therapy that follows successful induction therapy. It is designed to further intensify the treatment and help maintain the response achieved during induction. Consolidation therapy aims to eradicate any remaining cancer cells, reduce the risk of disease recurrence, and improve long-term outcomes.
- Induction Therapy: initial phase of treatment designed to rapidly reduce the burden of cancer cells in a patient's body. Its primary goal is to achieve remission or, in some cases, prepare the patient for additional therapies, such as stem cell transplantation.
- Line of Therapy:
    - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
    - Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
    - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.
- Refractory Disease: Illness or disease that does not respond to treatment.
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Approved Indications

Blyncito is indicated for the treatment of adult and pediatric patients with:

- 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%.
- Relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adult and pediatric patients one month and older.
- Treatment of CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia (ALL) in the consolidation phase of multiphase chemotherapy in adult and pediatric patients one month and older.
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Other Uses

No additional uses. See Background section above.

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9039	Injection,1 microgram [Blincyto]

ICD-10 Procedure

ICD-10	Description
XW03351	Introduction of blinatumomab antineoplastic immunotherapy into peripheral vein, percutaneous approach, new technology group 1
XW04351	Introduction of blinatumomab antineoplastic immunotherapy into central vein, percutaneous approach, new technology group 1

ICD-10 Diagnosis

ICD-10	Description
C91.00-C91.02	Acute lymphoblastic leukemia [ALL]

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Blincyto® (blinatumomab)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of CD19+ B-cell precursor acute lymphoblastic leukemia (ALL); **AND**

ii. Individual is using for one of the following (Label, NCCN 1, NCCN 2A):

A. Relapsed or refractory disease; **OR**

B. Minimal residual disease (MRD) greater than or equal to 0.1%, following a first or second complete response to induction therapy; **OR**
C. As consolidation therapy (NCCN 2A);

OR

iii. Blinatumomab is used as maintenance therapy as a single agent alternating with POMP (prednisone, vincristine, methotrexate, and mercaptopurine) (NCCN 2A);

OR

iv. Individual has Philadelphia chromosome-negative (Ph-) status, confirmed by genetic testing; **AND**
v. Individual is in the consolidation phase of multiphase chemotherapy for ALL.

OR

vi. Individual is using Blinatumomab in combination with Interfant regimens for infant acute lymphoblastic leukemia (ALL) with KMT2A status (11q23) rearranged (NCCN 2A).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Blincyto therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity or disease progression while on the current regimen, and the recommended duration of therapy has not been exceeded. The following information should be submitted for reauthorization:
   A. A current oncology note documenting the patient's response to treatment showing no progression of disease
   B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

I. Initial Approval Duration: Per Cycle
II. Reauthorization Approval Duration: Per Cycle

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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i. Treatment of diffuse large B-Cell lymphoma (DLBCL); **OR**
ii. When the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indication.

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

For more information regarding quantity limitations, please visit CMS LCD L33794 available at: LCD - External Infusion Pumps (L33794) (cms.gov)

Indication	Cycle	Dosing schedule	Treatment Duration
MRD-positive B-cell Precursor ALL	Cycle 1 for Induction, followed by 3 additional cycles for consolidation (42 days)	Patients weighing 45 kg or more (Fixed Dose): 28 mcg/day on Days 1-28, followed by 14-day treatment-free interval. Patients weighing 45 kg or less (BSA-based dose, not to exceed 28 mcg/day): 15 mcg/m^2/day on Days 1-28, followed by 14-day treatment-free interval	Up to 4 cycles
Relapsed or Refractory B-cell Precursor ALL	Up to 2 cycles for induction followed by 3 additional cycles for consolidation and up to 4 additional cycles of continued therapy. Cycles Duration: Induction Cycles 1 and 2 and Consolidation Cycles 3-5: 28 days of	**Induction Cycle 1:** - Days 1-7: ○ Patients weighing 45 kg or more (Fixed Dose): 9 mcg/day ○ Patients weighing 45 kg or less (BSA-based dose, not to exceed 9mcg/day): 5 mcg/m^2/day - Days 8-28 (followed by 14-day treatment-free interval):	Up to 9 cycles of treatment (induction cycles 1-2, consolidation cycles 3-5, and continued therapy cycles 6-9)

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Indication	Cycle	Dosing schedule	Treatment Duration
	continuous intravenous infusion followed by a 14-day treatment-free interval (total 42 days). <u>Consolidation Cycles 6-9:</u> 28 days of continuous intravenous infusion followed by a 56-day treatment-free interval (total 84 days).	○ Patients weighing 45 kg or more (Fixed Dose): 28 mcg/day. ○ Patients weighing 45 kg or less (BSA-based dose, not to exceed 28 mcg/day): 15 mcg/m^2/day **<u>Induction Cycle 2 and Consolidation Cycles 3-5:</u>** - Patients weighing 45 kg or more (Fixed Dose): 28 mcg/day on Days 1-28, followed by 14-day treatment-free interval. - Patients weighing 45 kg or less (BSA-based dose, not to exceed 28 mcg/day): 15 mcg/m^2/day on Days 1-28, followed by 14-day treatment-free interval **<u>Consolidation Cycles 6-9:</u>** - Patients weighing 45 kg or more (Fixed Dose): 28 mcg/day on Days 1-28, followed by 56-day treatment-free interval. - Patients weighing 45 kg or less (BSA-based dose, not to exceed 28 mcg/day): 15 mcg/m^2/day on Days 1-28, followed by 56-day treatment-free interval	
Consolidation Phase of B-cell precursor ALL	Single cycle of Blincyto monotherapy for 28 days of continuous intravenous infusion followed by a 14-day treatment-free interval (total 42	- Patients weighing 45 kg or more (Fixed Dose): 28 mcg/day on Days 1-28, followed by 14-day treatment-free interval. - Patients weighing 45 kg or less (BSA-based dose, not to exceed 28 mcg/day): 15 mcg/m^2/day on Days 1-28, followed by 14-day	Up to 4 cycles integrated with chemotherapy cycles.

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Indication	Cycle	Dosing schedule	Treatment Duration
	days).	treatment-free interval.	
Exceptions			
None			

Reference Information

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 18, 2023.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Foa R, Bassan R, Vitle A, et al. Dasatinib-blinatumumab for Ph-positive acute lymphoblastic leukemia in adults. N Engl J Med 2020; 383:1613-1623.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information, visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 18, 2023.
    a. Pediatric Acute lymphoblastic Leukemia. V1.2023. Revised November 9, 2022.
    b. Acute Lymphoblastic Leukemia. V1.2022. Revised April 4, 2022.
6. Medicare Coverage Data Base. (10/01/2015). Local Coverage Determination: External Infusion Pumps (L33794). Revision effective date: 07/01/2023. Retrieved from *LCD - External Infusion Pumps (L33794) (cms.gov)*.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Added new indication for Philadelphia Chromosome-Negative B-cell Precursor ALL in the Consolidation Phase and recommended dosing schedule. Update criteria to allow consolidation, maintenance therapy, and in combination with interfant regimens or mini-hyper CVD per NCCN; remove exclusion for CNS involvement and first line therapy per NCCN, include treatment as consolidation or for relapsed/refractory disease as a single agent or in combination per NCCN; update combination with interfant regimens to include KMT2A status (11q23) rearranged per NCCN. Coding Reviewed: No changes.	11/18/2024	12/17/2024
Annual Review	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	3/25/2024	5/9/2024
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 10/18/24.