Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Blinatumomab (Blyncito®)	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).

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 relapsed or refractory B-cell precursor ALL as well as B-cell ALL in first or second complete remission with minimal residual disease (MRD) great than or equal to 0.1%. The National Comprehensive Cancer Network® (NCCN) guidelines include additional 2A recommendations for the use of Blincyto in combination with certain tyrosine kinase inhibitors (TKIs) including bosutinib, dasatinib, imatinib, nilotinib, or ponatinib for Philadelphia chromosome-positive B-ALL. NCCN also recommends Blincyto in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) with Besponsa for relapsed or refractory disease 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. Interfant regimens include certain chemotherapy combination treatment protocols 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.

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.

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- 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).

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.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Blincyto® (blinatumomab)

A. Criteria For Initial Approval

i. Individual has a diagnosis of CD19+ B-cell precursor acute lymphocytic leukemia (ALL); **AND**
ii. Blinatumomab is used as a single agent (Label); **AND**
iii. Individual is using for one of the following:
   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

iv. Individual has a diagnosis of CD19+ B-cell precursor acute lymphocytic leukemia (ALL) (NCCN 2A); **AND**

v. Blinatumomab is used in combination with a tyrosine kinase inhibitor (bosutinib, dasatinib, imatinib, nilotinib, or ponatinib) (NCCN 2A); **AND**

vi. Individual is using for one of the following (NCCN 2A):

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

B. As consolidation therapy;

OR

vii. Individual has a diagnosis of CD19+ B-cell precursor acute lymphocytic leukemia (ALL) (NCCN 2A); **AND**

viii. Blinatumomab is used in combination with mini-hyper CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) with Besponsa; **AND**

ix. Individual is using for relapsed or refractory disease;

OR

x. Individual has a diagnosis of CD19+ B-cell precursor acute lymphocytic leukemia (ALL) (NCCN 2A); **AND**

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

OR

xii. Individual is using Blinatumomab in combination with Interfant regimens for infant acute lymphocytic leukemia (ALL) (NCCN 2A).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Blyncito 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.

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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):

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)

Drug	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.	**Induction Cycle 1:** - Days 1-7: ○ Patients weighing 45 kg or more (Fixed Dose): 9 mcg/day	Up to 9 cycles of treatment (induction cycles 1-2, consolidation cycles 3-5, and continued therapy cycles 6-9)

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Drug	Cycle	Dosing schedule	Treatment Duration
	Cycles Duration: <u>Induction Cycles 1 and 2 and Consolidation Cycles 3-5:</u> 28 days of 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 less (BSA-based dose, not to exceed 9mcg/day): 5 mcg/m^2/day <u>Days 8-28 (followed by 14-day treatment-free interval):</u> ○ 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	

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Drug	Cycle	Dosing schedule	Treatment Duration
		Days 1-28, followed by 56-day 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	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023

Revised: 11/08/2023