POLICY NUMBER UM_1270	**SUBJECT** Blincyto™ (blinatumomab)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 4**
DATE REVIEWED 03/02/15, 05/19/16, 06/29/17, 07/03/18, 06/07/19	**APPROVAL DATE** June 12, 2019	**EFFECTIVE DATE** June 12, 2019	**REVISION DATES** (latest version listed last) 03/02/15, 03/27/15, 05/24/16, 07/26/17, 07/19/18, 06/12/19	
PRIMARY BUSINESS OWNER: **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Blincyto (blinatumomab) usage in the treatment of cancer.

II. DEFINITIONS

Blincyto (blinatumomab): is a CD3 T-cell engager that binds to CD19 expressed on the surface of B-cell precursors and to CD3 expressed on the surface of T cells. When CD3 in the T-cell receptor complex connects to CD19 on B-cells, endogenous T cells are activated and cause the lysis of CD19+ cells.

Blincyto (blinatumomab) is FDA approved for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) or in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%.

Blincyto (blinatumomab) is available as 35 mcg of lyophilized powder in a single-use vial for reconstitution.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Blincyto (blinatumomab) may be considered medically necessary when any of the following selection criteria is met:

1. **Acute Lymphoblastic Leukemia (ALL)**
    - **a.** Blincyto (blinatumomab) is being used as a single agent as consolidation therapy for members with minimal residual disease positive (MRD+) following a complete response to induction therapy **OR**
    - b. The member has relapsed/refractory B-cell ALL and Blincyto (blinatumomab) is being used as a single agent for the following conditions:
        - i. Philadelphia chromosome-negative disease **OR**
        - ii. Philadelphia chromosome-positive disease refractory to tyrosine kinase inhibitor therapy (i.e. imatinib, nilotinib, or dasatinib) **AND**
        - iii. Relapse/refractory is defined as any of the following:

1) With first remission </= 12 months **OR**
2) After first salvage therapy **OR**
3) Within 12 months of allogeneic hematopoietic stem cell transplantation (HSCT).

Exclusion Criteria: Blincyto (blinatumomab) is not considered medically necessary when any of the following selection criteria is met:

1. Disease progression while taking Blincyto (blinatumomab).
2. Concurrent use with other chemotherapy, immunotherapy, or tyrosine kinase inhibitors (i.e. imatinib, nilotinib, or dasatinib)
3. Dosing exceeds single dose limit of Blincyto (blinatumomab) 28 mcg.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Blincyto (blinatumomab) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**
    a. Cycle 1 (weight 45 kg or greater): 9 mcg/day continuous IV infusion on days 1 through 7 and 28 mcg/day continuous IV infusion on days 8 through 28; 4 weeks continuous IV infusion followed by at least 2 weeks of no treatment; pre-medicate with dexamethasone 20 mg IV 1 hour before the first blinatumomab dose of each cycle, before a step dose (e.g., cycle 1 day 8), or when restarting an infusion after an interruption of 4 or more hours.
    b. For cycles 2 to 9 (weight 45 kg or greater): 28 mcg IV daily for 28 consecutive days/cycle
    c. Repeat induction (cycles 1 and 2) and consolidation (cycles 3 to 5) treatment cycles every 42 days; repeat cycles 6 to 9 (maintenance treatment) every 84 days.
    d. Pre-medicate with dexamethasone 20 mg at 1 hour prior to the first dose of each cycle, prior to a dosage increase (e.g., day 8 of cycle 1), and prior to resuming therapy (after stopping for 4 or more hours).
2. **Dosage Adjustments**
    a. Cytokine release syndrome, grade 3: Withhold treatment until resolved; restart at 9 mcg/day for 7 days, then increase to 28 mcg/day if toxicity has not recurred; if treatment interruption is 7 days or less, continue the same cycle to a total of 28 days, including the days before and after the interruption; if treatment interruption is longer than 7 days, start a new cycle.
    b. Cytokine release syndrome, grade 4: Permanently discontinue treatment.
    c. Neurotoxicity, grade 3: Withhold treatment until grade 1 or less for at least 3 days; restart at 9 mcg/day for 7 days, then increase to 28 mcg/day if toxicity has not recurred; if toxicity occurred at 9 mcg/day or does not resolve in 7 days or less, permanently discontinue treatment; if treatment interruption is 7 days or less, continue the same cycle to a total of 28 days, including the days before and after the interruption; if treatment interruption is longer than 7 days, start a new cycle.

d. Neurotoxicity, grade 4: Permanently discontinue treatment.

e. Seizure: Permanently discontinue treatment if more than 1 seizure occurs.

f. Adverse reaction, clinically relevant grade 3: Withhold treatment until grade 1 or less; restart at 9 mcg/day for 7 days, then increase to 28 mcg/day if adverse reaction has not recurred; if not resolved in 14 days or less, permanently discontinue treatment; if treatment interruption is 7 days or less, continue the same cycle to a total of 28 days, including the days before and after the interruption; if treatment interruption is longer than 7 days, start a new cycle.

g. Adverse reaction, clinically relevant grade 4: Consider permanent discontinuation.

3. **Monitoring**

a. Complete remission or complete remission with partial hematological recovery indicates efficacy.

b. Signs and symptoms of cytokine release syndrome, including associated conditions of DIC, capillary leak syndrome, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome.

c. Signs and symptoms of infusion reaction, which may be clinically indistinguishable from cytokine release syndrome.

d. Signs and symptoms of infection..

e. Signs and symptoms of tumor lysis syndrome.

f. Laboratory parameters, including WBC and absolute neutrophil count; during infusion.

g. ALT, AST, gamma-glutamyl transferase, and total blood bilirubin; before and during treatment.

h. Signs and symptoms of neurotoxicity.

i. Pancreatitis: Evaluate patients who develop signs and symptoms of pancreatitis. Management of pancreatitis may require either temporary interruption or discontinuation.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Blincyto prescribing information. Amgen, Inc. Thousand Oaks, CA. 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.

5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.