Blinatumomab (Blincyto®)

NDC CODE(S) 55513-0160-XX BLINCYTO 35MCG Solution Reconstituted (AMGEN)

DESCRIPTION

Blinatumomab is the first immunotherapy approved by the FDA to activate the body's own T-cells to fight disease. T-cells are types of white blood cells or lymphocytes which are natural parts of the immune system. Functionally, blinatumomab is a bispecific CD19-directed CD3 T- cell engager.

The B-lymphocyte antigen CD19 is found on the surface of B-cells throughout all stages of their development. CD19 is present on both benign and malignant B-cells and has been found to be an effective target for antineoplastic agents.

The CD3 antigen or T-cell co-receptor is a protein complex is found on the surface of T-cells. It is comprised of four distinct immunoglobulin chains and a single immunoreceptor tyrosine-based activation motif (ITAM). The transmembrane region of the chains is negatively charged and associates with the positively-charged T-cell receptor (TCR) molecule forming the TCR complex. This complex generates the signal for T-cell proliferation and activation.

Blinatumomab selectively binds to CD19 molecules on the surface of CD19+ B-cell lymphoblasts and to the CD3 on T-cells causing proliferation of T-cells through the action of the TCR complex. The outcome is upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines and proliferation of T-cells leading to destruction of malignant B-cells such as those of leukemia.

POLICY

- Blinatumomab for the treatment of acute lymphoblastic leukemia (ALL) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Blinatumomab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 1 month old; **AND**

Universal Criteria

- Used as single agent therapy; **AND**
- Patient has not received a live vaccine within 2 weeks prior to initiating therapy and will not receive concurrent treatment with lives vaccine while on therapy; **AND**

B-Cell Precursor Acute Lymphocytic Leukemia (ALL)

- Patient has relapsed or refractory disease (Philadelphia chromosome [Ph]-positive patients must be TKI intolerant/refractory); **OR**
- Used as consolidation therapy in patients with minimal residual disease positive (MRD+) following a complete response/remission to induction therapy; **OR**
- Used in patients that are MRD+ after consolidation therapy; **OR**
- Used in patients that are Ph-positive with less than complete response after induction therapy

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: Cytokine Release Syndrome (CRS), neurological toxicities, serious infections, pancreatitis, tumor lysis syndrome, neutropenia/febrile neutropenia, elevated liver enzymes, leukoencephalopathy, etc.; **AND**
- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH; **AND**
  - Patient has not exceeded 4 cycles of continued therapy or 9 total cycles of therapy for the treatment of relapsed or refractory disease; **OR**
  - Continued therapy for use in the treatment of MRD+ ALL may not be renewed.

DOSAGE/ADMINISTRATION

INDICATION	DOSE

Acute Lymphoblastic Leukemia	**Relapsed/Refractory Disease***
	• Weight greater than or equal to 45 kg
	  ○ Cycle 1 (induction):
	  ▪ 9 mcg daily x 7 days, then 28 mcg daily x 21 days in a 42 day cycle
	  ○ Cycles 2-5 (induction/consolidation):
	  ▪ 28 mcg daily x 28 days in a 42 day cycle
	  ○ Cycles 6-9 (continued therapy):
	  ▪ 28 mcg daily x 28 days in an 84 day cycle
	• Weight less than 45 kg
	  ○ Cycle 1 (induction) :
	  ▪ 5 mcg/m2/day (not to exceed 9 mcg/day) x 7 days, then 15 mcg/m2/day (not to exceed 28 mcg/day) x 21 days in a 42 day cycle
	  ○ Cycles 2-5 (induction/consolidation):
	  ▪ 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle
	  ○ Cycles 6-9 (continued therapy):
	  ▪ 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in an 84 day cycle
	*Up to 9 total cycles of therapy.

	MRD+ Disease*
	• Weight greater than or equal to 45 kg
	  ○ Cycle 1 (induction) :
	  ▪ 28 mcg daily x 28 days in a 42-day cycle
	  ○ Cycles 2-4 (consolidation):
	  ▪ 28 mcg daily x 28 days in a 42 day cycle
	• Weight less than 45 kg
	  ○ Cycle 1 (induction) :
	  ▪ 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle
	  ○ Cycles 2-4 (consolidation):
	  ▪ 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle
	*Up to 4 total cycles of therapy.

LENGTH OF AUTHORIZATION

- Relapsed or Refractory B-Cell Precursor Acute Lymphocytic Leukemia (ALL)
  - Initial coverage will be provided for 30 weeks for a total of five cycles (2 cycles of induction followed by 3 cycles of consolidation)
  - Continued coverage will be provided every 24 weeks for a maximum of two additional authorizations (4 cycles of continued therapy)
- MRD+ B-Cell Precursor Acute Lymphocytic Leukemia (ALL)
  - Initial coverage will be provided for 24 weeks for a total of four cycles (1 cycle of induction followed by 3 cycles of consolidation)
  - Continued coverage may not be renewed

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- Relapsed or Refractory B-Cell Precursor Acute Lymphocytic Leukemia (ALL)
  - Cycle 1 – 5 (Induction/Consolidation)
    - 980 billable units per 42 days
  - Cycle 6 – 9 (Continued Therapy)
    - 980 billable units per 84 days
- MRD+ B-Cell Precursor Acute Lymphocytic Leukemia (ALL)
  - Cycle 1 – 4 (Induction/Consolidation)
    - 980 billable units per 42 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Blincyto [package insert]. Thousand Oaks, CA; Amgen, March 2020. Accessed February 2021.

2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) blinatumomab. National Comprehensive Cancer Network, 20210. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
3. Jen EY, Xu Q, Schetter A, Przepiorka D, et al. FDA Approval: Blinatumomab for Patients with B-cell Precursor Acute Lymphoblastic Leukemia in Morphologic Remission with Minimal Residual Disease. Clin Cancer Res. 2019 Jan 15;25(2):473-477. doi: 10.1158/1078-0432.CCR-18-2337. Epub 2018 Sep 25.
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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Pediatric Acute Lymphoblastic Leukemia 2.20210. National Comprehensive Cancer Network, 20210. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
7. Topp MS, Gökbuget N, Stein AS, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. Lancet Oncol. 2015;16(1):57-66.
8. von Stackelberg A, Locatelli F, Zugmaier G, et al. Phase I/Phase II Study of Blinatumomab in Pediatric Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia. J Clin Oncol. 2016;34(36):4381-4389.
9. Lexicomp Online. (2020, March). AHFS DI. *Blinatumomab.* Retrieved June 23, 2020 from Lexicomp Online with AHFS.
10. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, March). *Blinatumomab*. Retrieved June 23, 2020 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/30/2021

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