VENTURA COUNTY HEALTH CARE PLAN

Utilization Review Policy

POLICY: Oncology – Blincyto® (blinatumomab injection for intravenous use – Amgen)

APPROVAL DATE: 09/04/2019

OVERVIEW

Blincyto binds to CD19 expressed on the surface of B-cells and to CD3 on the surface of T-cells.[1] This results in the activation of T-cells by connecting CD3 in the T-cell receptor complex with CD19 on benign and malignant B-cells. This leads to the development of a synapse between the T-cell and the B-cell, upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T-cells, which ultimately leads to redirected lysis of CD19 positive B-cells.

Blincyto, a bispecific CD19-directed CD3 T-cell engager, is indicated for the treatment of adults and children with:

- B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) $\geq$ 0.1%.[1] Accelerated approval was granted for this indication based on MRD response and hematologic relapse-free survival. Continued approval may be dependent on verification and description of clinical benefit in confirmatory trials.
- Relapsed or refractory B-cell ALL.[1]

Blincyto contains a boxed warning for Cytokine Release Syndrome which may be life-threatening or fatal and Neurologic toxicities which may be severe, life-threatening or fatal.[1] Stop or discontinue Blincyto as recommended for either toxicity.

Dosing in Minimal Residual Disease Positive B-Cell Precursor ALL. For patients $\geq$ 45 kg (99 lbs), the dose of Blincyto is 28 mcg/day on Days 1 through 28 of each cycle. For patients < 45 kg (99 lbs), the dose is 15 mcg/m^2/day, not to exceed 28 mcg/day on Days 1 through 28 of each cycle. A maximum of 4 cycles of Blincyto is recommended for minimal residual disease positive B-cell precursor ALL. A course of treatment consists of 1 induction cycle followed by 3 consolidation cycles. Each cycle consists of a 28-day continuous intravenous infusion of Blincyto followed by a 14-day treatment-free interval. A treatment course may take 6 to 9 months to complete.[1]

Dosing in Relapsed/Refractory B-Cell Precursor ALL. In patients < 45 kg (99 lbs), Blincyto is dosed based on body surface area. The recommended dose in Cycle 1 is 5 mcg/m^2/day (not to exceed 9 mcg/day) on Days 1 through 7 and 15 mcg/m^2/day (not to exceed 28 mcg/day) on Days 8 through 28. In subsequent cycles the recommended dose is 15 mcg/m^2/day (not to exceed 28 mcg/day) on Days 1 through 28. A maximum of 9 cycles of Blincyto is recommended for relapsed/refractory B-cell precursor ALL. A treatment course of Blincyto consists of up to 2 induction cycles, 3 consolidation cycles and up to 4 additional cycles. A cycle of induction or consolidation therapy consists of a 28-day continuous intravenous infusion followed by 14-day treatment-free interval. A single course of continued therapy consists of a 28-day continuous intravenous infusion followed by 56-day treatment-free interval.[1]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on Acute Lymphoblastic Leukemia (version 2.2019 – May 15, 2019) and Pediatric Acute Lymphoblastic Leukemia (version 1.2020 – May 30, 2019) recommend Blincyto as single-agent therapy for relapsed/refractory B-cell ALL; consolidation therapy in adolescents, young adults, and adults with positive MRD after complete response to induction therapy; and for pediatric patients with MRD positive disease, less than complete response, or high-risk genetics.[2-4]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Blincyto. Approval is recommended for those who meet the conditions of coverage for **Criteria** and **Dosing**. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Blincyto, as well as the monitoring required for adverse events and long-term efficacy, approval requires Blincyto to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Blincyto is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Acute Lymphoblastic Leukemia. Approve for 1 year if the patient meets the following criteria (A, B, and C):
- **A)** Blincyto is prescribed by or in consultation with an oncologist; AND
- **B)** The patient has B-cell precursor disease; AND
- **C)** The patient meets one of the following (i or ii):
  - **i.** The patient is Philadelphia chromosome negative and meets one of the following (a or b):
    - **a)** The patient has relapsed or refractory disease; OR
    - **b)** The patient is minimal residual disease positive; OR
  - **ii.** The patient is Philadelphia chromosome positive and meets one of the following (a, b, c, or d):
    - **a)** The patient has tried at least one tyrosine kinase inhibitor (TKI) used for the treatment of acute lymphoblastic leukemia (NOTE: Examples of a TKI include Gleevec® [imatinib tablets], Sprycel® [dasatinib tablets], Tasigna® [nilotinib capsules]); OR
    - **b)** The patient does not have a complete response to induction therapy; OR
    - **c)** The patient is minimal residual disease positive; OR
    - **d)** The patient has high-risk genetics.[2-4]

Dosing. Approve the following dosing regimen (A, B and C):
- **A)** Each individual dose must not exceed 28 mcg/day administered by intravenous infusion; AND
- **B)** The dose is administered on Days 1 through 28 of each treatment cycle; AND
- **C)** There is a minimum of a 14-day treatment-free interval between cycles.[1]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Blincyto has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Blincyto® injection for intravenous use [prescribing information]. Thousand Oaks, CA: Amgen; March 2018.

2. The NCCN Pediatric Acute Lymphoblastic Leukemia Oncology Guidelines (Version 1.2020 – May 30, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 17, 2019.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 17, 2019.
4. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 17, 2019. Search term: blinatumomab.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	--	09/19/2018
Annual	Combined Relapsed or Refractory criteria with Minimal Residual Disease criteria under Acute Lymphoblastic Leukemia. ALL: Added criteria for Philadelphia chromosome positive disease if the patient does not have a complete response to induction therapy, has minimal residual disease, or high-risk genetics. Revised "TKI intolerant or refractory" to "has tried a TKI." Increased duration of approval for minimal residual disease to 1 year. Removed Other Cancer Indications, and Waste Management sections.	09/04/2019