CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Blinatumomab (Blincyto®)

Version: 2.0

EFFECTIVE DATE: 1/1/2024

NantHealth® | Eviti®

Please note the following:

Blinatumomab (Blincyto®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Blinatumomab (Blincyto): Discussion

Blinatumomab is a type of immunotherapy called a bispecific CD19-directed CD3 T-cell engager (BiTE). It simultaneously attaches to T cells and cancer cells, enabling T cells to easily find and destroy the cancer cell by bringing them closer together. During this process, T cells are activated, creating more killer T cells.[1]

Blinatumomab is approved by the Food and Drug Administration (FDA) for the treatment of:

CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adults, characterized by MRD-positive status with minimal residual disease (MRD) greater than or equal to 0.1% in first or second complete remission, is approved under accelerated approval based on MRD response rate and hematological relapse-free survival.

Blinatumomab is indicated for the treatment of relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in adults.[2]

Blinatumomab is associated with several adverse reactions including Cytokine Release Syndrome, Neurological Toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome, Infections, Tumor Lysis Syndrome, Neutropenia and Febrile Neutropenia, Elevated Liver Enzymes, Pancreatitis and Leukoencephalopathy.

Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving blinatumomab. This happens when the immune system responds to infection or immunotherapy drugs more aggressively than it should. CRS symptoms include fever, nausea, fatigue, and body aches. Prompt treatment is essential, as symptoms can worsen quickly. Neurological toxicities, which may be severe, life-threatening, or fatal, occurred in patients receiving blinatumomab. Interrupt or discontinue blinatumomab as recommended.[2]

The National Comprehensive Cancer Network (NCCN) endorses blinatumomab in the following cancer types: acute lymphoblastic leukemia and pediatric acute lymphoblastic leukemia.[3,4]

Blinatumomab: Definitions

- **CD19 Mutation –** A change in the DNA sequence of a cell that can cause a type of hypogammaglobulinemia in which the response of mature B cells to antigenic stimulation is defective.
- **ECOG1910 regimen** – A randomized phase 3 study that evaluated blinatumomab immunotherapy in patients with a good prognosis after an initial round of chemotherapy. The goal of the E1910 trial was to further improve overall survival in patients with a better prognosis, defined as in complete remission and MRD negative (<0.01%), by bringing blinatumomab into the front-line setting.[5]
- **Food and Drug Administration (FDA)** – The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Minimal residual disease (MRD) -** A term used to describe a very small number of cancer cells that remain in the body during or after treatment.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Precursor B-lymphoblastic leukemia -** An aggressive (fast-growing) type of leukemia (blood cancer) in which too many B-cell lymphoblasts (immature white blood cells) are found in the bone marrow and blood.
- **Tyrosine kinase inhibitor (TKI)** - A substance that blocks the action of enzymes called tyrosine kinases. Tyrosine kinases are a part of many cell functions, including cell signaling, growth, and division. These enzymes may be too active or found at high levels in some types of cancer cells and blocking them may help keep cancer cells from growing. Some tyrosine kinase inhibitors are used to treat cancer. They are a type of targeted therapy.

Blinatumomab: Policy

Note: Coverage of blinatumomab will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation OR when all criteria are met.

Blinatumomab will be considered for coverage when the following criteria are met:

For **FDA** required criteria coverage:

Acute Lymphoblastic Leukemia

1. At least one month of age; AND
2. Prescribed by or in consultation with an oncologist; AND

3. Treatment of 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%; OR
4. Treatment of relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL); OR
5. Treatment of CD19-positive Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia (ALL) in the consolidation phase of multiphase chemotherapy.[2]

For **NCCN** required criteria coverage:

Acute Lymphoblastic Leukemia

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Therapy as a component of ECOG1910 regimen (preferred in frontline for adults age <65 years without substantial comorbidities) for one of the following:
   a) Induction phase 1 (daunorubicin, vincristine, prednisone, pegaspargase); and induction phase 2 (cyclophosphamide, cytarabine, mercaptopurine); with rituximab if CD20-positive + blinatumomab. This regimen is used for Philadelphia chromosome negative B-ALL for one of the following:
      i) During frontline therapy
      ii) During refractory therapy in adults aged ≥65 years or adults with substantial comorbidities
      iii) As a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline; OR
4. Therapy for Philadelphia chromosome-positive B-ALL for one of the following:
   a) With or without a Tyrosine kinase inhibitor (TKI) during frontline consolidation therapy if persistent/rising minimal residual disease (MRD) after a complete response (CR) to induction therapy
   b) With a TKI during frontline consolidation therapy if MRD negative after CR to induction therapy if not a candidate for multiagent therapy
   c) May be considered if refractory to TKIs: as a component of inotuzumab ozogamicin + mini-hyper-CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) + blinatumomab during induction/consolidation therapy
   d) May be considered if refractory to TKIs: alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone) as maintenance therapy if negative minimal residual disease (MRD) or MRD unavailable after a complete response (CR) to inotuzumab ozogamicin + mini-hyper-CVD
   e) With or without a (CD19 antigen directed) TKI during relapsed/refractory therapy; OR
5. Therapy for Philadelphia chromosome-negative B-ALL for one of the following:
   a) During consolidation therapy if persistent/rising minimal residual disease (MRD)
   b) During consolidation therapy if MRD negative/unavailable and induced with inotuzumab ozogamicin + mini-hyper-CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine)

c) During consolidation therapy if multiagent therapy is contraindicated
d) Alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone) during maintenance therapy if induced with inotuzumab ozogamicin + mini-hyper-CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine)
e) As a component of inotuzumab ozogamicin + mini-hyper-CVD (cyclophosphamide, dexamethasone, vincristine, methotrexate, cytarabine) + blinatumomab during relapsed/refractory therapy
f) As a CD19 antigen-directed single agent during relapsed/refractory therapy; OR

6. Consolidation therapy as a single agent if minimal/measurable residual disease negative/unavailable as a component of ALLIANCE A041703. The above regimen is used for adults aged ≥65 years or adults with substantial comorbidities with Philadelphia chromosome-negative B-ALL with one of the following:
   a) During frontline therapy
   b) During refractory therapy
   c) As a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline.[3]

Note:

1. TKI options include: bosutinib, dasatinib, imatinib, nilotinib, or ponatinib
2. Imatinib use in first line should be restricted to those who cannot tolerate broader acting TKIs
3. TKI/mutation contraindications: Bosutinib - T315I, V299L, G250E, or F317L; Dasatinib - T315I/A, F317L/V/I/C or V299L; Imatinib too numerous to include; Nilotinib - T315I, Y253H, E255K/V, F359V/C/I or G250E

Pediatric Acute Lymphoblastic Leukemia

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Single-agent therapy for one of the following:
   a) Ph-negative or Ph-like B-ALL that is minimal residual disease positive and negative incorporated into frontline consolidation therapy
   b) Ph-negative or Ph-like B-ALL that is minimal residual disease positive and negative after intensified consolidation therapy
   c) Ph-negative or Ph-like B-ALL that is minimal residual disease negative (MRD-) after intensified consolidation therapy incorporated into continuation of frontline consolidation therapy
   d) Ph-positive B-ALL with standard risk and low minimal residual disease incorporated into frontline consolidation therapy with imatinib or dasatinib
   e) Ph-positive B-ALL with high risk and less than complete response or minimal residual disease positive (MRD+) at end of consolidation incorporated into frontline consolidation therapy with imatinib or dasatinib
   f) Relapsed/refractory Ph-negative B-ALL
   g) Relapsed/refractory Ph-positive TKI intolerant/refractory B-ALL

Note: As a post-remission approach based on data from ECOG1910.

4. Therapy in combination with imatinib or dasatinib for Ph-positive B-ALL with high risk and less than complete response or minimal residual disease positive (MRD+) at the end of consolidation
5. Induction therapy in combination with interfant regimens for infant ALL with KMT2A status (11q23) rearranged
6. Therapy for relapsed/refractory Ph-negative B-ALL, or in combination with dasatinib or imatinib for relapsed/refractory Ph-positive B-ALL as a component of COG AALL1331 regimen.[4]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Blinatumomab: References

1. Trial Suggests Expanded Role for Blinatumomab in Treating ALL. https://www.cancer.gov/news-events/cancer-currents-blog/2023/blincyto-leukemia-minimal-residual-disease. Accessed on June 12, 2024.
2. Blincyto®(blinatumomab) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125557s021lbl.pdf. Accessed June 12, 2024.
3. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed June 12, 2024.
4. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed June 12, 2024.
5. ECOG-ACRIN cancer research group, Press Release: Practice-changing trial results for acute lymphoblastic leukemia (ALL). https://ecog-acrin.org/press-release-practice-changing-trial-results-for-acute-lymphoblastic-leukemia-all/. Accessed June 12, 2024.

Blinatumomab: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

CODE	DESCRIPTION
C83.50-C83.59, C91.00-C91.02	Acute Lymphoblastic Leukemia
C91.00-C91.01	Pediatric Acute Lymphoblastic Leukemia
J9039	Blinatumomab (Blincyto)

Blinatumomab: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	6/29/2023, 6/12/2024.
3	Policy Revision Dates:	6/12/2024
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	7/20/2023, 7/31/2024
6	Revision Changes:	6/12/2024 Addition of adverse reactions, enhanced discussion section, and added 2 indications in ALL and pediatric ALL