CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Epcoritamab-bysp (Epkinly™)

Version: 1.0

EFFECTIVE DATE: 12/1/2024

NantHealth® | Eviti®

Please note the following:

Epcoritamab-bysp (Epkinly®)

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.

Epcoritamab-bysp (Epkinly): Discussion

Epcoritamab-bysp is a T-cell engaging bispecific IgG1 (Immunoglobulin G1) antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and healthy B-lineage cells. In vitro, epcoritamab-bysp activate T-cells cause the release of proinflammatory cytokines, and induce lysis of B-cells.[1]

Epcoritamab-bysp interacts with the CD3 receptor that is expresses on the surface of T cells as well as the CD20 receptor that is expressed on the surface of lymphoma cells and healthy B-lineage cells triggering lysis of B-cells, activate T-cells, and the release of proinflammatory cytokines. [2]

Epcoritamab-bysp adverse reactions (≥ 20% of patients) include cytokine release syndrome, fatigue, musculoskeletal pain, injection site reactions, pyrexia, abdominal pain, nausea, diarrhea, COVID -19, upper respiratory tract infection, rash, cough, and headache.
The most common grade 3 to 4 laboratory abnormalities (≥ 10% of patients) include decreased lymphocyte, neutrophils, white blood cell, hemoglobin, and platelet counts.

Epcoritamab-bysp is approved by the Food and Drug Administration (FDA) for treatment of diffuse large B-cell lymphoma (DLBCL), B-cell lymphoma and follicular lymphoma.[1]

The National Comprehensive Cancer Network (NCCN) endorses epcoritamab-bysp in the following cancer types: classic follicular lymphoma, diffuse large B-cell lymphoma, histologic transformation of indolent lymphomas, high-grade B-cell lymphomas, HIV-related B-cell lymphomas, and post-transplant lymphoproliferative disorders.[3]

Epcoritamab-bysp: Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than thirty 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.
- **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.

- **CD3 Receptor (Cluster of Differentiation 3)** - A protein complex and T cell co-receptor that plays a crucial role in the activation and signal transduction of T cells. It is composed of four distinct chains: two CD3ε, one CD3γ, and one CD3δ. These chains associate with the T-cell receptor (TCR) and the CD3-zeta (ζ) chain to form the TCR complex, which is essential for T cell activation.[4]
- **CD20 Receptor** - A protein found on the surface of B cells, a type of white blood cell. It plays a crucial role in the immune system and is often used as a marker to identify B cells.[5]

Epcoritamab-bysp: Policy

Note: Coverage of epcoritamab-bysp 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.

Epcoritamab-bysp will be considered for coverage when the following criteria are met:

B-Cell Lymphomas

Classic Follicular Lymphoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Relapsed or refractory disease after two or more lines of systemic therapy[1]; OR

For **NCCN** required criteria coverage:

4. Subsequent therapy for partial response, no response, relapsed, or progressive disease in patients with indications for treatment.[3]

Diffuse Large B-Cell Lymphoma/Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma/High-Grade B-Cell Lymphomas

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Relapsed or refractory diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy[1]; OR

For **NCCN** required criteria coverage:

4. Subsequent therapy (only after at least two lines of systemic therapy) as a single agent for partial response, no response, progressive, relapsed, or refractory disease.[3]

HIV-Related B-Cell Lymphomas

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Subsequent therapy (only after at least two lines of systemic therapy) as a single agent for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma, for partial response, relapsed, progressive, or refractory disease.[3]

Post-Transplant Lymphoproliferative Disorders

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Subsequent therapy (only after at least two lines of systemic therapy) for monomorphic PTLD (B-cell type) as a single agent for partial response, relapsed, progressive or refractory disease.[3]

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

Epcoritamab-bysp: References

1. Epcoritamab-bysp. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761324s003lbl.pdf. Accessed November 20, 2024.
2. Riaz et al. Epcoritamab-bysp (Epkinly) – A phenomenal breakthrough in the treatment of diffuse large B-cell lymphoma. https://pmc.ncbi.nlm.nih.gov/articles/PMC10392166/. Accessed November 20, 2024.
3. National Comprehensive Cancer Network. B-cell Lymphomas. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed November 20, 2024.

4. Ngoenkam et al. Selected signalling proteins recruited to the T-cell receptor-CD3 complex. https://pubmed.ncbi.nlm.nih.gov/28771705/. Accessed November 20, 2024.
5. National Cancer Institute. CD20. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cd20. Accessed November 20, 2024.

Epcoritamab-bysp: 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
C82.9	Classic Follicular Lymphoma
C83.3	Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas
C85.1	Other B-Cell Lymphomas
D47.Z1	Post-Transplant Lymphoproliferative Disorders
J9321	Epcoritamab-bysp

Epcoritamab-bysp: Revision and Review History

No.	Description	Dates(s)
1	Original Effective Date:	12/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	12/21/2024
6	Revision Changes:	