CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Loncastuximab Tesirine-lpyl (Zynlonta®)

Version: 1.0

EFFECTIVE DATE: 5/5/2025

NantHealth® | Eviti®

Please note the following:

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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.

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.

Loncastuximab Tesirine-lpyl (Zynlonta®)

Discussion

Loncastuximab tesirine-Ipyl is an antibody-drug conjugate (ADC) targeting CD19. The monoclonal immunoglobulin G1 (IgG1) kappa antibody component binds to human CD19, a transmembrane protein expressed on the surface of B-lineage cells. The small molecule component is SG3199, a PBD dimer and alkylating agent. Upon binding to CD19, loncastuximab tesirine-lpyl is internalized, followed by release of SG3199 via proteolytic cleavage. The released SG3199 binds to the DNA minor groove and forms highly cytotoxic DNA interstrand crosslinks, subsequently inducing cell death.[1,2]

Adverse reactions associated with loncastuximab tesirine-lpyl include effusion, edema, myelosuppression, cutaneous reactions, embryo fetal toxicity, thrombocytopenia, increased gamma-glutamyltransferase, neutropenia, anemia, hyperglycemia, transaminase elevation, fatigue, hypoalbuminemia, rash, edema, nausea, and musculoskeletal pain.[1]

Loncastuximab tesirine-Ipyl is approved by the Food and Drug Administration (FDA) and National Comprehensive Cancer Network (NCCN) for B-cell lymphoma.[1,3]

Definitions

- **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.[4]
- **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.[5]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

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 large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma;[1] OR

Classic Follicular Lymphoma

For **NCCN** required criteria coverage:

4. Third-line and subsequent therapy in combination with rituximab for partial response, no response, relapsed, or progressive disease;[3] OR

Diffuse Large B-Cell Lymphoma

For **NCCN** required criteria coverage:

5. Third-line and subsequent therapy as a single agent for partial response, relapsed, progressive or refractory disease;[3] OR

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

For **NCCN** required criteria coverage:

6. If previously treated with an anthracycline-based regimen and there is no intention for the patient to proceed to transplant, then it can be given for one of the following:
   a) Additional therapy for partial response, no response, progressive, or relapsed disease following chemoimmunotherapy for histologic transformation after minimal or no prior therapy
   b) After multiple lines of prior therapies, including ≥2 chemoimmunotherapy regimens for indolent disease prior to histologic transformation;[3] OR

High-Grade B-Cell Lymphomas

For **NCCN** required criteria coverage:

7. Third-line and subsequent therapy as a single agent for partial response, no response, relapse, progressive or refractory disease; OR

HIV-Related B-Cell Lymphomas

For **NCCN** required criteria coverage:

8. Third-line and subsequent therapy as a single agent for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma, not otherwise specified for partial response, relapsed, progressive or refractory disease[3]; OR

Post-Transplant Lymphoproliferative Disorders

For **NCCN** required criteria coverage:

9. Third-line and subsequent 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

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	Follicular lymphoma
C83.3	Diffuse large B-cell lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder
J9359	Injection, loncastuximab tesirine-lpyl

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	5/5/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	5/5/2025
6	Revision Changes:	

References

[1] Loncastuximab tesirine-lpyl (Zynlonta) [Package Insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761196s004s005lbl.pdf. Accessed April 9, 2025.

[2] Lee A. Loncastuximab Tesirine: First Approval. *Drugs*. 2021;81(10):1229-1233. https://pubmed.ncbi.nlm.nih.gov/34143407/. Accessed April 9, 2025.

[3] National Comprehensive Cancer Network. NCCN Guidelines: B-Cell Lymphomas. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed April 9, 2025.

[4] U.S. Food & Drug Administration. https://www.fda.gov/about-fda/what-we-do. Accessed April 23, 2025.

[5] National Comprehensive National Cancer Network. https://www.nccn.org/home. Accessed April 23, 2025.