

Medical Drug Clinical Criteria

Subject: Zynlonta (loncastuximab tesirine-lpyl)
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Overview

This document addresses the use of Zynlonta (loncastuximab tesirine-lpyl). Zynlonta is a monoclonal antibody-drug conjugate (ADC) that consists of an IgG1 antibody specific for CD19 and a small molecule component including an alkylating agent. The anticancer activity is due to the binding of the ADC to CD19-expressing cells and cleavage of alkylating component which induces cell death. The target CD19 is a surface protein found on B-cells and Zynlonta is indicated to treat diffuse large B-cell lymphoma (DLBCL). Post-Transplant Lymphoproliferative Disorders is treated the same way as relapsed/refractory DLBCL per National Comprehensive Cancer Network (NCCN).

The FDA approved indication for Zynlonta includes adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. The indication includes diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, and high-grade B-cell lymphoma. Zynlonta is approved under accelerated approval based on overall response rate; continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Definitions and Measures

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Monoclonal antibody: A protein developed in the laboratory that can locate and bind to specific substances in the body and on the surface of cancer cells.

Non-Hodgkin Lymphoma (NHL): A group of malignant solid tumors or lymphoid tissues.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Zynlonta (loncastuximab tesirine-lpyl)

Requests for Zynlonta (loncastuximab tesirine-lpyl) may be approved if the following criteria are met:

- I. Individual has a diagnosis of no response, partial response, progressive, relapsed or refractory large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low grade lymphoma, HIV-related diffuse large B-cell lymphomas (NCCN 2A), and high-grade B-cell lymphomas, and Post-Transplant Lymphoproliferative Disorders;
- AND
- II. Individual is using Zynlonta as a single agent; **AND**
- III. Individual has received at least two prior lines of systemic therapy; **AND**
- IV. Individual has a current ECOG performance status of 0-2 (NCT03589469).

Requests for Zynlonta (loncastuximab tesirine-lpyl) may not be approved for the following:

- I. All other indications not included above; **OR**
- II. Individuals with active central nervous system (CNS) lymphoma.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9359 Injection, loncastuximab tesirine-lpyl, 0.075 mg [Zynlonta]

ICD-10 Diagnosis

- C83.30 Diffuse large B-cell lymphoma, unspecified site
- C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
- C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes
- C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
- C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
- C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
- C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes
- C83.37 Diffuse large B-cell lymphoma, spleen
- C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
- C83.39 Diffuse large B-cell lymphoma, extranodal and solid organ sites
- B20 Human immunodeficiency virus [HIV] disease
- C83.30-C83.38 Diffuse large B-cell lymphoma
- C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

<u>C83.80-C83.89</u>	<u>Other non-follicular lymphoma</u>
<u>C85.10-C85.19</u>	<u>Unspecified B-cell lymphoma</u>
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

Document History

Revised: 08/15/2025

Document History:

- 08/15/2025 – Annual Review: Add no response and partial response disease, remove ECOG score. Coding Reviewed: Removed ICD-10-CM C83.39. Consolidated codes C83.30-C83.38 into one range and updated description. Added ICD-10-CM B20, C83.398, C83.80-C83.89, C85.10-C85.19, C85.20-C85.29.
- 08/16/2024 – Annual Review: No Change. Coding Reviewed: Added ICD-10-CM D47.Z1 for PTLD to align with NCCN 2A criteria addition 8/18/2023.
- 08/18/2023 – Annual Review: Update language from AIDs to HIV and add Post-Transplant Lymphoproliferative Disorders. Coding Reviewed: No changes.
- 08/19/2022 – Annual Review: Update large B-cell lymphoma criteria. Coding reviewed: Removed ICD-10-CM C83.30-C83.39. Added ICD-10-CM C83.30, C83.31, C83.32, C83.33, C83.34, C83.35, C83.36, C83.37, C83.38, C83.39.
- 05/21/2021 – Annual Review: Add new clinical criteria document for Zynlonta. Coding reviewed: Added HCPCS J3490, J3590, J9999. All diagnoses pend. Effective 10/1/2021 Added HCPCS C9084, Added ICD-10-CM C83.30-C83.39. Added ICD-10-CM Description Diffuse large B-Cell lymphoma. Effective 4/1/2022 Added HCPCS J9359. Removed C9084, J3490, J3590, J9999. Removed all diagnoses pend.

References

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 - a. B-cell Lymphomas. V2.2025. Revised February 10, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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