

Zynlonta® (loncastuximab tesirine-lpyl) (Intravenous)

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I. Length of Authorization

- Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Zynlonta 10 mg single-dose powder for injection: 2 vials every 21 days for the first two doses followed by 1 vial every 21 days thereafter

B. Max Units (per dose and over time) [HCPCS Unit]:

- B-Cell Lymphomas
 - Cycles 1 and 2: 230 billable units (17.25 mg) per each 21 day cycle
 - Subsequent Cycles: 115 billable units (8.63 mg) per each 21 day cycle

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria ¹

- Used as a single agent; **AND**
- Patient has not received prior anti-CD19 therapy, (e.g., tafasitamab, CAR-T) OR patient previously received anti-CD19 therapy and re-biopsy indicates CD-19 positive disease; **AND**
- Patient does not have active graft-versus-host disease; **AND**
- Patient has not had an autologous stem cell transplant (ASCT) within 30 days or allogeneic stem cell transplant (AlloSCT) with 60 days, prior to start of therapy; **AND**
- Patient does not have active CNS lymphoma (*includes leptomeningeal disease*); **AND**
- Patient does not have a clinically significant active infection (e.g., Grade 3 or 4 infections); **AND**

- Patient does not have any clinically significant third space fluid accumulation (e.g., ascites requiring drainage or pleural effusion that is either requiring drainage or associated with shortness of breath); **AND**

B-Cell Lymphomas † ‡ ◊ ^{1,4}

- Diffuse Large B-Cell Lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, High-Grade B-Cell Lymphoma, HIV-related DLBCL, primary effusion lymphoma, or HHV8-positive DLBCL, not otherwise specified
 - Patient has received at least two prior lines of therapy; **AND**
 - Patient has had no response or partial response OR has relapsed, progressive, or refractory disease
- Histologic Transformation of Indolent Lymphomas* to Diffuse Large B-Cell Lymphoma (DLBCL) ‡
 - Patient has no intention to proceed to transplant; **AND**
 - Used as additional therapy for partial response, no response, or progressive disease following chemoimmunotherapy if the patient has histologic transformation to diffuse large B-cell lymphoma after minimal or no prior treatment; **OR**
 - Patient has received multiple prior therapies for indolent or transformed disease

**Indolent Lymphomas: extranodal marginal zone lymphoma (EMZL) of the stomach or nongastric sites (noncutaneous), splenic or nodal marginal zone lymphoma, or follicular lymphoma*

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); ◊ Orphan Drug

IV. Renewal Criteria ¹

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe effusion and edema (e.g., pleural effusion, pericardial effusion, ascites, peripheral edema, general edema, etc.), myelosuppression (e.g., neutropenia, thrombocytopenia, anemia, etc.), serious infections, severe cutaneous reactions (e.g., photosensitivity reaction, rash, erythema, etc.), etc.

V. Dosage/Administration ¹

| Indication | Dose |
|------------------|---|
| B-Cell Lymphomas | <ul style="list-style-type: none">Administer 0.15 mg/kg by intravenous infusion every 3 weeks for 2 cycles, then 0.075 mg/kg every 3 weeks for subsequent cycles until disease progression or unacceptable toxicity. <p><i>*For patients with a body mass index (BMI) ≥ 35 kg/m², calculate the dose based on an adjusted body weight (ABW) as follows: $ABW \text{ in kg} = 35 \text{ kg/m}^2 \times (\text{height in meters})^2$.</i></p> |

VI. Billing Code/Availability Information

HCPCS Code:

- J9359 – Injection, loncastuximab tesirine-lpyl, 0.075 mg; 1 billable unit = 0.075 mg

NDC:

- Zynlonta 10 mg single-dose powder for injection: 79952-0110-xx

VII. References

1. Zynlonta [package insert]. Murray Hill, NJ; ADC Therapeutics America. October 2022. Accessed January 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) loncastuximab tesirine. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2023.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for B-Cell Lymphomas Version 2.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2023.
4. ADC Therapeutics. A Phase 2 Open-Label Single-Arm Study to Evaluate the Efficacy and Safety of Loncastuximab Tesirine in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL) (LOTIS-2). Available from: <https://clinicaltrials.gov>. NLM identifier: NCT03589469. Accessed April 26, 2021.
5. Caimi PF, Ai W, Alderuccio JP, et al. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol* 2021; 22:790.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|---|
| 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 |
| C83.80 | Other non-follicular lymphoma, unspecified site |
| C83.81 | Other non-follicular lymphoma, lymph nodes of head, face, and neck |
| C83.82 | Other non-follicular lymphoma, intrathoracic lymph nodes |
| C83.83 | Other non-follicular lymphoma, intra-abdominal lymph nodes |
| C83.84 | Other non-follicular lymphoma, lymph nodes of axilla and upper limb |
| C83.85 | Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb |
| C83.86 | Other non-follicular lymphoma, intrapelvic lymph nodes |
| C83.87 | Other non-follicular lymphoma, spleen |
| C83.88 | Other non-follicular lymphoma, lymph nodes of multiple sites |
| C83.89 | Other non-follicular lymphoma, extranodal and solid organ sites |
| C83.90 | Non-follicular (diffuse) lymphoma, unspecified, unspecified site |
| C83.91 | Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck |
| C83.92 | Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes |
| C83.93 | Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes |
| C83.94 | Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb |
| C83.95 | Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb |
| C83.96 | Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes |
| C83.97 | Non-follicular (diffuse) lymphoma, unspecified, spleen |
| C83.98 | Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites |
| C83.99 | Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites |
| C85.10 | Unspecified B-cell lymphoma, unspecified site |
| C85.11 | Unspecified B-cell lymphoma, lymph nodes of head, face, and neck |
| C85.12 | Unspecified B-cell lymphoma, intrathoracic lymph nodes |

| | |
|--------|--|
| C85.13 | Unspecified B-cell lymphoma, intra-abdominal lymph nodes |
| C85.14 | Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb |
| C85.15 | Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C85.16 | Unspecified B-cell lymphoma, intrapelvic lymph nodes |
| C85.17 | Unspecified B-cell lymphoma, spleen |
| C85.18 | Unspecified B-cell lymphoma, lymph nodes of multiple sites |
| C85.19 | Unspecified B-cell lymphoma, extranodal and solid organ sites |
| C85.20 | Mediastinal (thymic) large B-cell lymphoma, unspecified site |
| C85.21 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck |
| C85.22 | Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes |
| C85.23 | Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes |
| C85.24 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb |
| C85.25 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C85.26 | Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes |
| C85.27 | Mediastinal (thymic) large B-cell lymphoma, spleen |
| C85.28 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites |
| C85.29 | Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites |
| C85.80 | Other specified types of non-Hodgkin lymphoma, unspecified site |
| C85.81 | Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck |
| C85.82 | Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes |
| C85.83 | Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes |
| C85.84 | Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C85.85 | Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb |
| C85.86 | Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes |
| C85.87 | Other specified types of non-Hodgkin lymphoma, spleen |
| C85.88 | Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites |
| C85.89 | Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions

| Jurisdiction | Applicable State/US Territory | Contractor |
|---------------------|---|---|
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |