Zynlonta™ (loncastuximab tesirine-lpyl)
(Intravenous)

-E-

Document Number: IC-0657

Last Review Date: 05/02/2022
Date of Origin: 02/01/2022
Dates Reviewed: 02/2022, 04/2022, 05/2022

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**
- Patient has been advised to minimize or avoid exposure to direct natural or artificial sunlight including exposure through glass windows; **AND**

Universal Criteria [1]

- Used as single agent therapy; **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 † ‡ Φ [1,4]

- Diffuse Large B-Cell Lymphoma (DLBCL), not otherwise specified, DLBCL arising from low grade lymphoma, or High-Grade B-cell Lymphoma †
    - 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 Nongastric (noncutaneous) or Gastric MALT Lymphoma, Splenic or Nodal Marginal Zone Lymphoma, or Follicular Lymphoma (grade 1-2) to Diffuse Large B-Cell Lymphoma (DLBCL) ‡
    - Patient has received at least two prior lines of chemoimmunotherapy for indolent or transformed disease (patients should have received at least one anthracycline or anthracenedione-based regimen, unless contraindicated)

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

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

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet 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, and general edema), myelosuppression (e.g., neutropenia, thrombocytopenia, and

anemia), serious infections, severe cutaneous reactions (e.g., photosensitivity reaction, rash, erythema), etc.

V. Dosage/Administration [1]

Indication	Dose
B-Cell Lymphomas	• 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. **For patients with a body mass index (BMI) ≥35 kg/m², calculate the dose based on an adjusted body weight (ABW) as follows: ABW in kg = 35 kg/m² × (height in meters)².*

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 (STANDARD)

1. Zynlonta [package insert]. Murray Hill, NJ; ADC Therapeutics, Inc. September 2021. Accessed April 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) loncastuximab tesirine. National Comprehensive Cancer Network, 2022. 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 April 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for B-Cell Lymphomas Version 2.2022. National Comprehensive Cancer Network, 2022. 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 April 2022.
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.

VIII. References (ENHANCED)

1e. 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 Jun;22(6):790-800. doi: 10.1016/S1470-2045(21)00139-X.

2e. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. N Engl J Med. 2019;380(1):45-56. doi:10.1056/NEJMoa1804980.

3e. Neelapu S, Locke F, Bartlett N, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med 2017; 377:2531-2544.

4e. Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. Lancet. 2020 Sep 19;396(10254):839-852. doi: 10.1016/S0140-6736(20)31366-0.

5e. Kalakonda N, Maerevoet M, Cavallo F, et al. Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial. Lancet Haematol. 2020 Jul;7(7):e511-e522. doi: 10.1016/S2352-3026(20)30120-4.

6e. Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma. J Clin Oncol. 2020 Jan 10;38(2):155-165. doi: 10.1200/JCO.19.00172.

7e. Salles G, Duell J, González Barca E, et al. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm, phase 2 study. Lancet Oncol. 2020 Jul;21(7):978-988. doi: 10.1016/S1470-2045(20)30225-4.

8e. Magellan Health, Magellan Rx Management. Zynlonta Clinical Literature Review Analysis. Last updated April 2022. Accessed April 2022.

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

C83.90	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
C85.20	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

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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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