

Epkinly™ (epcoritamab-bysp) (Subcutaneous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

- Epkinly 4 mg/0.8 mL single-dose vial: 1 vial on days 1 and 8 of cycle 1
- Epkinly 48 mg/0.8 mL single-dose vial: 1 vial on days 15 and 22 of cycle 1; days 1, 8, 15, 22 of cycles 2 and 3; days 1 and 15 of cycles 4 to 9; and day 1 of cycle 10 and beyond

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

B-Cell Lymphomas (28-day cycles)

- Cycle 1: 25 billable units on day 1, 25 billable units on day 8, 300 billable units on days 15 and 22
- Cycles 2 and 3: 300 billable units on days 1, 8, 15, 22
- Cycles 4 to 9: 300 billable units on days 1 and 15
- Cycles 10 and beyond: 300 billable units on day 1

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

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

Universal Criteria ¹

- Prophylaxis for infection will be followed according to local guidelines (e.g., *Pneumocystis jirovecii* pneumonia (PJP), *Herpes virus*, etc.); **AND**
- Patient does not have a clinically significant active systemic infection; **AND**
- Patient does not have primary central nervous system (CNS) lymphoma or CNS involvement of disease; **AND**
- Patient has not received prior allogeneic hematopoietic stem cell transplantation (HSCT); **AND**

- Used as a single agent; **AND**

B-Cell Lymphomas † ‡ ^{1,3,4}

- Used after at least two prior lines of systemic therapy; **AND**
 - Patient has diffuse large B-cell Lymphoma (DLBCL) (*including DLBCL, not otherwise specified*), high-grade B-cell lymphoma, HIV-related B-cell lymphoma (i.e., HIV-related DLBCL, primary effusion lymphoma, or HHV8-positive large B-cell lymphoma, not otherwise specified), or monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type); **AND**
 - Used for partial response, progressive, relapsed, or refractory disease; **OR**
 - Patient has histologic transformation of an indolent lymphoma (follicular lymphoma or marginal zone lymphoma) to DLBCL; **AND**
 - Used for partial response, no response, progressive, relapsed, or refractory disease

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ 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**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infections, serious or life-threatening cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS), severe cytopenias (including neutropenia, anemia, and thrombocytopenia), etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration ¹

Indication	Dose
B-Cell Lymphomas	Administer subcutaneously in 28-day cycles, until disease progression or unacceptable toxicity. <ul style="list-style-type: none"> • Cycle 1: <ul style="list-style-type: none"> – Step-up dose one: 0.16 mg on day 1 – Step-up dose two: 0.8 mg on day 8 – First full dose: 48 mg on day 15 <ul style="list-style-type: none"> • Patients should be hospitalized for 24 hours after administration of the first full 48 mg dose due to the risks of CRS and ICANS – 48 mg on day 22

	<ul style="list-style-type: none"> • Cycles 2 and 3: <ul style="list-style-type: none"> – 48 mg on days 1, 8, 15, 22 • Cycles 4 to 9: <ul style="list-style-type: none"> – 48 mg on days 1 and 15 • Cycles 10 and beyond: <ul style="list-style-type: none"> – 48 mg on day 1
<p><u>Note:</u></p> <ul style="list-style-type: none"> – <i>Must be administered by a healthcare professional with appropriate medical support to manage severe reactions such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).</i> – <i>Ensure adequate hydration before administering therapy. Premedicate before each dose in Cycle 1.</i> 	

VI. Billing Code/Availability Information

HCPCS Code:

- J9321 – Injection, epcoritamab-bysp, 0.16 mg; 1 billable unit = 0.16 mg

NDC(s):

- Epkinly 4 mg/0.8 mL single-dose vial: 82705-0002-xx
- Epkinly 48 mg/0.8 mL single-dose vial: 82705-0010-xx

VII. References

1. Epkinly [package insert]. Plainsboro, NJ; Genmab US, Inc.; May 2023. Accessed February 2024.
2. Hutchings M, Mous R, Clausen MR, et al. Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase ½ study. *Lancet*. 2021 Sep 25;398(10306):1157-1169. Doi: 10.1016/S0140-6736(21)00889-8. Epub 2021 Sep 8.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) epcoritamab. National Comprehensive Cancer Network, 2024. 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 February 2024.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas, Version 1.2024. National Comprehensive Cancer Network, 2024. 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 Guidelines, go online to NCCN.org. Accessed February 2024.

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 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
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
Z85.72	Personal history of non-Hodgkin lymphomas

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD,

or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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