Evolent Clinical Guideline 3148 for Breyanzi™ (lisocabtagene maraleucel)

Guideline Number:	Applicable Codes	
Evolent_CG_3148		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. *© 2021 - 2025 Evolent. All rights Reserved.*		
Original Date:	**Last Revised Date:**	**Implementation Date:**
March 2021	July 2025	July 2025

TABLE OF CONTENTS

STATEMENT

Purpose

To define and describe the accepted indications for Breyanzi (lisocabtagene maraleucel) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)

- Breyanzi (lisocabtagene maraleucel) may be used for the treatment of adult members with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least 2 prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor (i.e. ibrutinib, acalabrutinib, zanubrutinib) and a B-cell lymphoma 2 (BCL-2) inhibitor (i.e. venetoclax).

Diffuse Large B-Cell Lymphoma (DLBCL), confirmed CD-19 positive [Lymphoma sub-types include DLBCL not otherwise specified including DLBCL arising from indolent lymphoma, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B]

- Breyanzi (lisocabtagene maraleucel) may be used for the treatment of adult members with relapsed or refractory diffuse large B-cell lymphoma and the above sub-types, confirmed documentation of CD-19 positive disease, AND who have the following:

- Refractory disease to first line chemoimmunotherapy or relapse within 12 months of first line chemoimmunotherapy OR
- Relapse after first line chemoimmunotherapy AND are not eligible for hematopoietic stem cell transplantation (HSCT) OR
- Relapsed or refractory disease after 2 or more lines of systemic therapy.

Follicular Lymphoma

- Breyanzi (lisocabtagene maraleucel) may be used for the treatment of adult members with relapsed or refractory follicular lymphoma (FL) who have received 2 or more prior lines of systemic therapy.

Mantle Cell Lymphoma

- Breyanzi (lisocabtagene maraleucel) may be used for the treatment of adult members with relapsed or refractory mantle cell lymphoma who have received 2 or more prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor (i.e. ibrutinib, acalabrutinib, zanubrutinib).

CONTRAINDICATIONS/WARNINGS

- US Boxed Warning
  - Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving lisocabtagene maraleucel. Do not administer lisocabtagene maraleucel to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab with or without corticosteroids.
  - Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving lisocabtagene maraleucel, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with lisocabtagene maraleucel. Provide supportive care and/or corticosteroids as needed.
  - T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including lisocabtagene maraleucel.

EXCLUSION CRITERIA

- Disease progression during or after taking Breyanzi (lisocabtagene maraleucel) or another anti-CD19 CAR-T cell therapy [e.g., Kymriah (tisagenlecleucel) or Yescarta (axicabtagene ciloleucel)].
- Lack of confirmed documentation of CD-19 positivity in tumor cells.
- Treatment with Breyanzi (lisocabtagene maraleucel) exceeds the maximum limit of 110 X 10^6 CAR-positive viable T-cells.
- Treatment exceeds the maximum duration limit as one time administration.
- Investigational use of Breyanzi (lisocabtagene maraleucel) with an off-label indication

that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

- Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
- Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
- Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- Q2054 - Lisocabtagene maraleucel, up to 110 million autologous anti-cd19 car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
July 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1421 Breyanzi (lisocabtagene maraleucel) • Updated exclusion criteria • Updated references
July 2024	• Added mantle cell lymphoma section to indication section • Added new reference

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Kamdar M, et al; TRANSFORM Investigators. Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial. *Lancet*. 2022 Jun 18;399(10343):2294-2308. doi: 10.1016/S0140-6736(22)00662-6.
2. Wang M, et al. Lisocabtagene Maraleucel in Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis of the Mantle Cell Lymphoma Cohort From TRANSCEND NHL 001, a Phase I Multicenter Seamless Design Study. *J Clin Oncol*. 2024 Apr 1;42(10):1146-1157. doi: 10.1200/JCO.23.02214.

3. Abramson JS, 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.
4. Siddiqi T, et al. Lisocabtagene maraleucel in chronic lymphocytic leukaemia and small lymphocytic lymphoma (TRANSCEND CLL 004): a multicentre, open-label, single-arm, phase 1-2 study. *Lancet*. 2023 Aug 19;402(10402):641-654. doi: 10.1016/S0140-6736(23)01052-8.
5. Morschhauser F, et al. Lisocabtagene maraleucel in follicular lymphoma: the phase 2 TRANSCEND FL study. *Nat Med*. 2024 Aug;30(8):2199-2207. doi: 10.1038/s41591-024-02986-9.
6. Breyanzi prescribing information. Juno Therapeutics, Inc. Bothell, WA 2025.
7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
12. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
13. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.