Molina Clinical Policy
Breyanzi (lisocabtagene maraleucel)
Policy No. 400

Last Approval: 08/13/2025
Next Review Due By: August 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

POLICY DESCRIPTION

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.

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 and/or LIMITATIONS OF COVERAGE

A. Continuation requests for a not-approvable medication shall be exempt from this policy provided:

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

B. 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]

1. 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:
   a. Refractory disease to first line chemoimmunotherapy or relapse within 12 months of first line chemoimmunotherapy OR
   b. Relapse after first line chemoimmunotherapy AND are not eligible for hematopoietic stem cell transplantation (HSCT) OR
   c. Relapsed or refractory disease after 2 or more lines of systemic therapy.

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

1. 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).

D. Follicular Lymphoma

1. 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.

E. Mantle Cell Lymphoma

1. 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

1. 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.
2. 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.
3. 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

A. 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)].

B. Lack of confirmed documentation of CD-19 positivity in tumor cells.

C. Treatment with Breyanzi (lisocabtagene maraleucel) exceeds the maximum limit of 110 X 10^6 CAR-positive viable T-cells.

D. Treatment exceeds the maximum duration limit as one time administration.

E. 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:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. 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.)
5. 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.

6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

APPLICABLE CPT / HCPCS PROCEDURE CODES

CPT (Current Procedural Terminology)

Code	Description
38225	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

AVAILABLE DOSAGE FORMS: Breyanzi is supplied in vials as separate frozen suspensions of each CD8 and CD4 component; each component is packed in a carton containing up to 4 vials, depending upon the concentration of the cryopreserved drug product CAR-positive vial T cells.

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/13/2025	Added contraindications (US Boxed Warning) and updated continuation criteria.
08/14/2024	Added indication for follicular lymphoma and updated references.
06/12/2024	Added indications for treatment of adult members with relapsed or refractory CLL or SLL who have received 2 prior lines of therapy including a BTK and BCL-2 inhibitor.
04/10/2024	Changes to exclusion criteria include removing following conditions: member not having adequate bone marrow reserve, and member not having adequate renal, hepatic, and cardiac function.
08/09/2023	Changes to indications/inclusion criteria to remove reference to preferred drug listing, and additional qualifications in section B for Diffuse Large B-Cell Lymphoma. Exclusion criteria revised to add section B and removed a few criteria. Updated code descriptions for codes 0537T, 0538T, 0539T, and 0540T. Reviewed by board certified Oncologist.
08/10/2022	Adopted NCH policy and retired MCP.

REFERENCES

1. Kamdar M, et al. TRANSFORM Clinical Trial. 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.
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.
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. Epub 2023 Jun 6. PMID: 37295445.
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.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

This policy contains prior authorization requirements.