Drug Policy:

Breyanzi™ (lisocabtagene maraleucel)

POLICY NUMBER UM ONC_1421	**SUBJECT** Breyanzi™ (lisocabtagene maraleucel)		**DEPT/PROGRAM** UM Dept	**PAGE 1 of 3**
DATES COMMITTEE REVIEWED 03/10/21, 05/12/21, 11/15/21, 02/09/22, 05/11/22, 09/14/22, 07/12/23, 02/14/24, 04/10/24, 06/12/24	**APPROVAL DATE** June 12, 2024	**EFFECTIVE DATE** June 28, 2024	**COMMITTEE APPROVAL DATES** 03/10/21, 05/12/21, 11/15/21, 02/09/22, 05/11/22, 09/14/22, 07/12/23, 02/14/24, 04/10/24, 06/12/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to 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.

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

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

D. 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 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.
    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.

IV. MEDICATION MANAGEMENT

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

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. 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.

B. 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.

C. 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.

D. A study to evaluate the efficacy and safety of JCAR017 in adult subjects with relapsed or refractory indolent B-cell non-Hodgkin lymphoma (NHL) (TRANSCEND FL). ClinicalTrials.gov. Updated November 30, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04245839

E. Breyanzi prescribing information. Juno Therapeutics, Inc. Bothell, WA 2024.

F. 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.

G. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.