STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

# Breyanzi (lisocabtagene maraleucel)
## PAM–039

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| **Iowa Medicaid Program:** | Prior Authorization | **Effective Date:** | 10/01/2021 |
| **Revision Number:** | 3 | **Last Rev Date:** | 10/20/2023 |
| **Reviewed By:** | Medicaid Medical Director | **Next Rev Date:** | 10/18/2024 |
| **Approved By:** | Medicaid Clinical Advisory Committee | **Approved Date:** | 10/15/2021 |

## Overview

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|---|---|
| Medication:[1] | lisocabtagene maraleucel |
| Brand Name: | Breyanzi® |
| Pharmacologic Category: | Antineoplastic agent, CAR-T immunotherapy. |
| FDA-Approved Indication(s): | CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B who have:<br>• refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy; or<br>• refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age; or<br>• relapsed or refractory disease after two or more lines of systemic therapy.<br>Limitations of Use: Breyanzi is not indicated for the treatment of patients with primary central nervous system (CNS) lymphoma. |
| How Supplied: | Genetically modified autologous T cells supplied in vials as separate frozen suspensions of each CD8 component and CD4 component. Each CD8 or CD4 component is packed in a carton containing up to 4 vials, depending upon the concentration of the cryopreserved drug product CAR-positive viable T cells. |
| Dosage and Administration: | • For autologous use only. For intravenous use only.<br>• Relapsed or refractory LBCL after one line of therapy:<br>  ○ A single dose contains 90 to 110 × $10^6$ CAR-positive viable T cells (consisting of 1:1 CAR-positive viable T cells of the CD8 and CD4 components).<br>• Relapsed or refractory LBCL after two or more lines of therapy:<br>  ○ A single dose contains 50 to 110 × $10^6$ CAR-positive viable T cells (consisting of 1:1 CAR-positive viable T cells of the CD8 and CD4 components). |
| Benefit Category: | Medical |

| BOXED WARNING: Cytokine release syndrome and neurologic toxicities |
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| **Cytokine Release Syndrome (CRS)**, including fatal or life-threatening reactions, occurred in patients receiving Breyanzi®. Do not administer 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 Breyanzi®, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment. Provide supportive care and/or corticosteroids as needed. |
| ➢ Breyanzi® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS. |

## Descriptive Narrative

Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL) accounting for approximately 25 percent of NHL cases in the developed world. In the United States, the incidence of DLBCL is approximately 7 cases per 100,000 persons per year. Incidence varies by ethnicity, with White Americans having higher rates than Black, Asian, and American Indian or Alaska Native individuals, in order of decreasing incidence. Like most other NHLs, there is a male predominance with approximately 55 percent of cases occurring in men. Incidence increases with age; the median age at presentation is 64 years for patients as a whole but appears to be younger for Black compared with White Americans.[2]

Patients with untreated relapsing or refractory aggressive B-cell lymphoma have a median survival of approximately 3 to 4 months. Outcomes tend to be especially poor with DLBCL that is refractory or relapses early after autologous HSCT. In a meta-analysis of over 500 such patients, objective response rates (ORRs) to subsequent therapy were 20 to 30 percent, complete remission (CR) rates were less than or equal to 15 percent, and the median overall survival (OS) was 6 months.[3]

## Definitions

- **CAR T-cell therapy:** A type of treatment in which a patient's T cells taken from a patient's blood are changed in the laboratory so they will attack cancer cells. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added to the T cells in the laboratory. The special receptor is called a chimeric antigen receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion.
- **Chemotherapy:** The medical treatment of a disease, particularly cancer, with drugs or other chemicals.
- **Chemoimmunotherapy:** A treatment option for cancer that combines traditional chemotherapy with immunotherapy. This approach aims to increase the efficacy of cancer treatment by simultaneously targeting cancer cells through chemotherapy and boosting the immune system's ability to fight cancer through immunotherapy.[4]

- **Line of therapy:**
  - First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy, or a combination of these therapies.
  - Second-line therapy: Treatment given when the initial treatment (first-line therapy) is not effective or there is disease progression.
  - Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent (second-line therapy) treatments are not effective or there is disease progression.
- **Refractory disease:** illness or disease that does not respond to treatment.
- **Relapse or recurrence:** After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

## Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[5]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for B-Cell Lymphomas (Version 6.2023 – October 10, 2023).[6]

| NCCN Guidelines® Recommendation(s) for lisocabtagene maraleucel (Breyanzi®) in DLBCL |
|---|
| (1) Second-line therapy [a, b, c]<br>A. No intention to proceed to transplant<br>i. lisocabtagene maraleucel: Category 2A, preferred<br>B. Relapsed disease < 12 months or primary refractory disease<br>i. lisocabtagene maraleucel: Category 1<br>(2) Third-line and subsequent therapy<br>A. Anti-CD19 CAR T-cell therapy (if not previously given)<br>i. lisocabtagene maraleucel: Category 2A<br>[a] Inclusion of any anthracycline or anthracenedione in patients with impaired cardiac functioning should have more frequent cardiac monitoring.<br>[b] If additional anthracycline is administered after a full course of therapy, careful cardiac monitoring is essential. Dexrazoxane may be added as a cardioprotectant.<br>[c] Rituximab should be included in second-line therapy if there is relapse after a reasonable remission (>6 mo); however; rituximab should often be omitted in patients with primary refractory disease. |

| NCCN Guidelines® Recommendation(s) for lisocabtagene maraleucel (Breyanzi®) in histological transformation of indolent lymphomas to DLBCL |
|---|
| (1) Systemic therapy regimens – anti-CD19 CAR T-cell therapy [d]<br>A. Histologic transformation of follicular lymphoma (FL) or marginal zone lymphoma (MZL) (all subtypes)<br>i. lisocabtagene maraleucel: Category 2A |

[d] Patients should have received at least one anthracycline or anthracenedione-based regimen, unless contraindicated.

| **NCCN Categories of Evidence and Consensus** (all recommendations are category 2A unless otherwise indicated) | |
|---|---|
| Category 1 | Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. |
| Category 2A | Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. |
| Category 2B | Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate. |
| Category 3 | Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate. |

| **NCCN Categories of Preference** (all recommendations are considered appropriate) | |
|---|---|
| Preferred intervention | Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability. |
| Other recommended intervention | Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes. |
| Useful in certain circumstances | Other interventions that may be used for select patient populations (defined with recommendation). |

## Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[7]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

| GRADE | ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score] |
|---|---|
| 0 | Fully active, able to carry on all pre-disease performance without restriction. |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work. |
| 2 | Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours. |
| 3 | Capable of only limited self-care; confined to bed or chair more than 50% of waking hours. |
| 4 | Completely disabled; cannot carry on any self-care; totally confined to bed or chair. |
| 5 | Dead. |

## Criteria

Tocilizumab (Actemra®) may be required to manage cytokine release syndrome (CRS) or neurologic toxicities. HCPCS code J3262 suspends for claims review. If tocilizumab therapy is required, may be approved for up to 4 doses of 800 mg each.

Prior authorization is required.

Breyanzi® is considered medically necessary when **ALL** of the following are met:

1. Member has a diagnosis of one of the following large B-cell lymphomas (LBCL):
    a. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified; **OR**
    b. DLBCL arising from indolent lymphoma; **OR**
    c. High-grade B-cell lymphoma; **OR**
    d. Primary mediastinal large B-cell lymphoma (PMBCL); **OR**
    e. Follicular lymphoma grade 3B; **OR**
    f. HIV related B-cell lymphomas (NCCN 2A): **OR**
    g. Monomorphic post-transplant lymphoproliferative (B-cell type) disorders (PTLD) (NCCN 2A); **AND**
2. Member is 18 years of age or older; **AND**
3. Request is for one of the following (a, b, or c):
    a. Member has refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy [which included an anti-CD20 monoclonal antibody (e.g., rituximab) and an anthracycline-containing chemotherapy regimen (e.g., doxorubicin]; or,
    b. Member has refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and is not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age; or
    c. Member has relapsed or refractory disease after two or more lines of systemic therapy [which included an anti-CD20 monoclonal antibody (e.g., rituximab) and an anthracycline-containing chemotherapy regimen (e.g., doxorubicin]; **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1; **AND**
5. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
6. Member does **NOT** have primary central nervous system lymphoma; **AND**
7. Member has **NOT** received any previous treatment with chimeric antigen receptor (CAR) T-cell immunotherapy or other genetically modified T-cell therapy (e.g., Abecma®, Carvykti®, Kymriah®, Tecartus®, or Yescarta®), nor will CAR T therapy or other genetically modified T-cell therapy be administered concurrently with Breyanzi®; **AND**
8. Member is receiving Breyanzi® as a one-time, single administration treatment; **AND**
9. Treatment will be administered at a facility that is certified under the Breyanzi® Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
10. Request meets one of the following (a or b):
    a. Diagnosis of r/r LBCL after one line of therapy and dose does not exceed 90 to 110 x $10^6$ CAR-positive viable T cells; or
    b. Diagnosis of r/r LBCL after two or more lines of therapy and dose does not exceed 50 to 110 x $10^6$ CAR-positive viable T cells.

Continued therapy will not be authorized, as Breyanzi® is indicated to be dosed one time only.

## Approval Duration and Quantity Limits

| | Initial Authorization | Subsequent Authorization |
|---|---|---|
| Approval Duration | One course of treatment per lifetime | Not applicable |
| Quantity Limits | One-time dose, not to exceed 110 x $10^6$ CAR-positive T cells | |

## Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

| HCPCS | Description |
|---|---|
| J3262 | Injection, tocilizumab, 1 mg [Actemra®: may be required to manage cytokine release syndrome or neurologic toxicities] |
| Q2054 | Lisocabtagene maraleucel, up to 110 million autologous anti-cd19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose |

| ICD-10 | Description |
|---|---|
| C82.40 – C82.49 | Follicular lymphoma grade IIIb |
| C83.30 – C83.39 | Diffuse large B-cell lymphoma |
| C83.90 – C83.99 | Non-follicular (diffuse) lymphoma |
| C85.20 – C85.29 | Mediastinal (thymic) large B-cell lymphoma |

| NDC | Labeler | Dosage | Pkg Size | Pkg Qty | Units/ Pkg |
|---|---|---|---|---|---|
| 73153-0901-08 (CD8) | Juno Therapeutics, Inc. | per treatment dose | 1 | EA | 1 |
| 73153-0902-04 (CD4) | Juno Therapeutics, Inc. | per treatment dose | 1 | EA | 1 |

## Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

## References

[1] Breyanzi® prescribing information (06/2023). Juno Therapeutics, Inc.: Bothell, WA. Available online at: www.breyanzihcp.com. Accessed August 24, 2023.

[2] Freedman AS, Aster JC. Epidemiology, clinical manifestations, pathologic features, and diagnosis of diffuse large B cell lymphoma. Rosmarin AG, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed June 30, 2023.

[3] BLA Clinical Review Memorandum: STN 125714/0. Lisocabtagene maraleucel (JCAR017). U.S. Food and Drug Administration – Center for Biologics Evaluation and Research (CBER). Available online at https://www.fda.gov/vaccines-blood-biologics/cellular-gene- therapy-products/breyanzi-lisocabtagene-maraleucel. Accessed September 24, 2021.

[4] Sordo-Bahamonde C, Lorenzo-Herrero S, et al. Chemo-Immunotherapy: A New Trend in Cancer Treatment. Cancers (Basel). 2023 May 25;15(11):2912. PMID: 37296876.

[5] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas. V.6.2023 – October 10, 2023. Accessed October 12, 2023. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org.

[7] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

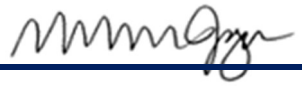
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

## Criteria Change History

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| | CAC | | |
| **Signature** | | | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 10/20/2023 | CAC | Annual review. Added boxed warning regarding cytokine release syndrome and neurologic toxicities to the Overview section. Updated DLBCL information in Descriptive Narrative. Added small list of definitions for various oncology terms. Updated NCCN Guidelines. Added paragraph before prior authorization criteria regarding tocilizumab (Actemra®) to manage CRS or neurological toxicities. Added dosing and therapy options into criteria. Added J3262 (Actemra®) to Coding and Product Information. | 3 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 10/21/2022 | CAC | New indications: 1. refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy.<br>2. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemo-immunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age. Updated NCCN Guidelines. | 2 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

| Change Date | Changed By | Description of Change | Version |
|---|---|---|---|
| 10/15/2021 | CAC | Criteria implementation. | 1 |
| **Signature**<br>William (Bill) Jagiello, DO | |  | |

CAC = Medicaid Clinical Advisory Committee