Utilization Review Policy 246A

POLICY: Oncology (Injectable – CAR-T) – Breyanzi Utilization Management Medical Policy
- Breyanzi® (lisocabtagene maraleucel intravenous infusion – Juno Therapeutics)

EFFECTIVE DATE: 06/01/2021
LAST REVISION DATE: 11/19/2025

COVERAGE CRITERIA FOR: UCare Medical Assistance and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

OVERVIEW

Breyanzi, a CD19-directed genetically modified autologous T-cell immunotherapy, is indicated for the treatment of:[1]

- **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, and follicular lymphoma grade 3B, in adults who have:[1]
  - Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy.
  - Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation due to age or comorbidities.
  - Relapsed or refractory disease after ≥ 2 lines of systemic therapy.

  Limitations of use: Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma.
- Relapsed or refractory **chronic lymphocytic leukemia** (CLL) or **small lymphocytic lymphoma** (SLL) in adults who have received at least two prior lines of therapy including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor.
- Relapsed or refractory **follicular lymphoma** in adults who have received two or more prior lines of systemic therapy.

  The CLL or SLL indication and follicular lymphoma indication are approved under accelerated approval based on response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Relapsed or refractory **mantle cell lymphoma** in adults who have received at least two prior lines of systemic therapy, including a BTK inhibitor.

Dosing Information

Breyanzi is supplied in separate frozen vials containing the CD8 component and the CD4 component.[1] Each component is supplied in cartons containing one to four vials depending on the concentration of the cryopreserved chimeric antigen receptor (CAR)-positive T-cells. The vials are stored in the vapor phase of liquid nitrogen ≤ -130°C. The dose of Breyanzi for relapsed or refractory LBCL after ≥ 2 lines of therapy is 50 to 110 x 10^6 CAR-positive viable T cells (consisting of a 1:1 mixture of the CD8 and CD4 components), with each component supplied separately in single-dose vials. The dose for relapsed or refractory LBCL after one line of therapy, CLL or SLL, follicular lymphoma, or mantle cell lymphoma is 90 to 110 x 10^6 CAR-positive viable T cells (consisting of a 1:1 mixture of the CD8 and CD4 components).

Guidelines

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines address Breyanzi:

- **B-Cell Lymphomas** (version 3.2025 – August 18, 2025) guidelines recommend Breyanzi for the treatment of a variety of lymphomas.[2,3] Breyanzi can be used as second-line and subsequent therapy for relapsed or refractory DLBCL, high-grade B-cell lymphoma, mantle cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, and post-transplant lymphoproliferative disorders. Breyanzi can also be used as third-line and subsequent therapy for classic follicular lymphoma and transformed indolent lymphoma to DLBCL.
- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma** (version 1.2026 – October 10, 2025) guidelines recommend Breyanzi for relapsed or refractory CLL/SLL in patients who have been treated with a BTK inhibitor and Venclexta® (venetoclax tablets) based regimens with or without del(17p)/T53 mutation (category 2A).[3,5] Breyanzi is also recommended for the treatment of histologic transformation to DLBCL in patients with del(17p)/TP53 mutation or who are chemotherapy refractory or unable to receive chemoimmunotherapy.
- **Pediatric Aggressive Mature B-Cell Lymphomas** (version 2.2025 – April 28, 2025) guidelines recommend Breyanzi for consolidation/additional therapy if the patient has achieved a partial response after treatment for relapsed/refractory primary mediastinal large B-cell lymphoma.[3,4] NCCN states this recommendation is based on extrapolation of results from clinical trials in adults with relapsed/refractory DLBCL including primary mediastinal large B-cell lymphoma.

Safety

Breyanzi has a Boxed Warning regarding cytokine release syndrome (CRS), neurologic toxicities, and T-cell malignancies.[1]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Breyanzi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Because of the specialized skills required for evaluation and diagnosis of patients treated with Breyanzi as well as the monitoring required for adverse events and long-term efficacy, approval requires Breyanzi to be prescribed by or in consultation with a physician who specializes in the condition being treated. The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Breyanzi is recommended in those who meet the following criteria:

FDA-Approved Indications

1. B-Cell Lymphoma. Approve a single dose if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** Patient meets BOTH of the following (a and b):
    - **a)** Patient has ONE of the following diagnoses [(1), (2), (3), (4), (5), (6), (7), (8), (9), or (10)]:
      - **(1)** Large B-cell lymphoma; OR

(2) Diffuse large B-cell lymphoma; OR
(3) High-grade B-cell lymphoma; OR
(4) Primary mediastinal large B-cell lymphoma; OR
(5) Follicular lymphoma, Grade 3B; OR
(6) Human immunodeficiency virus (HIV)-related diffuse large B-cell lymphoma; OR
(7) Human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma; OR
(8) Primary effusion lymphoma; OR
(9) Post-transplant lymphoproliferative disorders; OR
(10) Mantle cell lymphoma; AND

b) Patient has received at least one line of systemic therapy; OR

ii. Patient meets BOTH of the following (a and b):

a) Patient has ONE of the following diagnoses [(1) or (2)]:
(1) Transformed indolent lymphoma to diffuse large B-cell lymphoma; OR
(2) Classic follicular lymphoma; AND

b) Patient has received at least two lines of systemic therapy; AND

C) Patient has received or plans to receive lymphodepleting chemotherapy prior to infusion of Breyanzi; AND

D) Patient has not been previously treated with CAR-T therapy; AND
Note: Examples of CAR-T therapy includes Breyanzi, Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene intravenous infusion), and Yescarta (axicabtagene intravenous infusion).

E) The medication is prescribed by or in consultation with an oncologist.

Dosing. The dose is 50 to 110 x 10^6 CAR-positive viable T-cells administered intravenously as a single dose.

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2. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Approve a single dose if the patient meets ALL of the following (A, B, C, D, and E):

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. Patient meets ALL of the following (a, b, and c):

a) Patient has relapsed or refractory disease; AND

b) Patient has tried a Bruton tyrosine kinase inhibitor; AND
Note: Examples of Bruton tyrosine kinase inhibitors include Imbruvica (ibrutinib capsules and tablets), Calquence (acalabrutinib capsules and tablets), and Brukinsa (zanubrutinib capsule).

c) Patient has tried a B-cell lymphoma-2 (BCL-2) inhibitor; OR
Note: Examples of regimens containing BCL-2 inhibitor are Venclexta (venetoclax tablets), Venclexta + Gazyva (obinutuzumab intravenous infusion), Venclexta + rituximab, Venclexta + Imbruvica (ibrutinib capsules and tablets).

ii. Patient meets BOTH of the following (a and b):

a) Patient has histologic transformation to diffuse large B-cell lymphoma; AND

b) Patient meets ONE of the following [(1), (2), or (3)]:

(1) Patient has disease progression on non-chemoimmunotherapy regimen; OR
Note: Examples include Venclexta + Tecentriq (atezolizumab intravenous infusion) + Gazyva (obinutuzumab intravenous infusion), Opdivo (nivolumab intravenous infusion) ± ibrutinib, Keytruda (pembrolizumab intravenous infusion) ± ibrutinib, Jaypirca (pirtobrutinib tablets), Epkinly (epcoritamab-bysp subcutaneous injection),

Columvi (glofitamab-gxbm intravenous infusion), Brukinsa (zanubrutinib capsule) + Tevimbra (tislelizumab-jsgr intravenous infusion).

(2) Patient has refractory disease; OR

(3) Patient has had disease progression on chemoimmunotherapy; AND

Note: Examples of chemoimmunotherapy include dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, rituximab) and RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone).

C) Patient has received or plans to receive lymphodepleting chemotherapy prior to infusion of Breyanzi; AND

D) Patient has not been previously treated with CAR-T therapy; AND

Note: Examples of CAR-T therapy includes Breyanzi, Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene intravenous infusion), and Yescarta (axicabtagene intravenous infusion).

E) The medication is prescribed by or in consultation with an oncologist.

Dosing. The dose is 90 to 110 x 10^6 CAR-positive viable T-cells administered intravenously as a single dose.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Breyanzi is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Breyanzi® intravenous infusion [prescribing information]. Bothell, WA: Juno Therapeutics; June 2025.
2. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 3.2025 – August 18, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 17, 2025.
3. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 13, 2025. Search term: lisocabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – April 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 17, 2025.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2026 – October 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 17, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/18/2023
Annual Revision	**B-Cell Lymphoma:** Revised acquired immunodeficiency syndrome (AIDS) to human immunodeficiency virus (HIV).	01/17/2024
Selected Revision	**B-Cell Lymphoma:** Mantle cell lymphoma added as new condition of approval for patients who have received at least one prior line of therapy. Classic follicular lymphoma added as new condition of approval for patients who have received at least two prior lines of therapy. **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Added new condition of approval.	06/12/2024

UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Early Annual Revision	**Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Added new condition of approval that the patient has histologic transformation to diffuse large B-cell lymphoma and the patient has del(17p)/TP53 mutation or is chemotherapy refractory or unable to receive chemoimmunotherapy. Revised the dose to 90 to 110 x 10^6 CAR-positive viable T-cells.	11/13/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
Annual Revision	**Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** Added requirement patient has relapsed or refractory disease. In reference to trial of other therapies, changed wording from "patient has received" to "patient has tried" a Bruton tyrosine kinase inhibitor or B-cell Lymphoma-2 (BCL-2) inhibitor. For BCL-2 inhibitor requirement, added new Note with examples of Venclexta (venetoclax tablets) containing regimens. For requirements referring to histologic transformation to diffuse large B-cell lymphoma, the following changes were made: Deleted "Patient has del(17p)/TP53 mutation positive disease"; added "Patient has had disease progression on non-chemoimmunotherapy regimen" and included Note with examples; "Patient is chemotherapy refractory" has been modified to "Patient has refractory disease"; "Patient is unable to receive chemoimmunotherapy" has been modified to "Patient has disease progression on chemoimmunotherapy".	11/19/2025