Policy:	**Oncology (Injectable – CAR-T) – Breyanzi Utilization Management Medical Policy** • Breyanzi® (lisocabtagene maraleucel intravenous infusion – Juno Therapeutics)
Date:	02/09/2026
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	All States
Applicable NCDs, LCDs, and/or LCAs	NCD 110.24

SUMMARY OF EVIDENCE

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

- **Chronic lymphocytic leukemia** (CLL) or **small lymphocytic lymphoma** (SLL)**:** Treatment of relapsed or refractory disease 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.
- **Follicular lymphoma:** Treatment of relapsed or refractory disease 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.
- **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.
- **Mantle cell lymphoma:** Treatment of relapsed or refractory disease in adults who have received at least two prior lines of systemic therapy, including a BTK inhibitor.
- **Marginal zone lymphoma:** Treatment of relapsed or refractory disease in adults who have received at least two prior lines of systemic therapy.

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, marginal zone 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 1.2026 – December 22, 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 marginal zone lymphoma, 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]

ANALYSIS OF EVIDENCE

The information provided in the summary of evidence is supported by labeled indications, CMS-approved compendia, published clinical literature, clinical practice guidelines, and/or applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs). Refer to the Sources of Information section of this policy for additional information.

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. The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the Sources of Information section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Sources of Information section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference

purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are referenced in both the corresponding Standard Medical Utilization Management Internal Policy AND applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications may be internally developed and/or referenced in applicable NCDs, LCDs, and/or LCAs. For these indications, internally developed coverage criteria is denoted throughout the policy in the following manner: 1) IC-L (internal criteria supported by the labeled indication), 2) IC-COMP (internal criteria supported by CMS-approved compendia), 3) IC-ISGP (internal criteria intended to interpret or supplement general provisions outlined in applicable NCDs, LCDs, and/or LCAs), or 4) IC-EC (internal criteria intended to expand coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs). For these indications, coverage criteria that is NOT denoted with one of the above indicators is referenced in applicable NCDs, LCDs, and/or LCAs. Additional information supporting the rationale for determination of internal coverage criteria can be found via the Sources of Information section.

Indications with a @ below are referenced in the corresponding Standard Medical Utilization Management Internal Policy, but are NOT directly referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs). Coverage criteria for these indications is internally developed. These indications and their respective coverage criteria represent expanded coverage beyond the coverage outlined in applicable NCDs, LCDs, and/or LCAs.

Indications with a # below are supported and referenced in applicable National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and/or Local Coverage Articles (LCAs), but are NOT directly referenced in the corresponding Standard Medical Utilization Management Internal Policy. Coverage criteria for these indications is referenced in applicable NCDs, LCDs, and/or LCAs.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

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1. B-Cell Lymphoma. ^

Criteria. Approve a single dose if the patient meets the following criteria (A, B, C, and D):

A) 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; IC-COMP OR
    - **2)** Diffuse large B-cell lymphoma; IC-COMP OR
    - **3)** High-grade B-cell lymphoma; IC-COMP OR
    - **4)** Primary mediastinal large B-cell lymphoma; IC-COMP OR

5) Follicular lymphoma, Grade 3B; [IC-COMP] OR
6) Human immunodeficiency virus (HIV)-related diffuse large B-cell lymphoma; [IC-COMP] OR
7) Human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma; [IC-COMP] OR
8) Primary effusion lymphoma; [IC-COMP] OR
9) Post-transplant lymphoproliferative disorders; [IC-COMP] OR
10) Mantle cell lymphoma; [IC-COMP] AND

b) Patient has received at least one line of systemic therapy; [IC-COMP] OR

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

a) Patient has ONE of the following diagnoses [(1), (2) or (3)]:
1) Transformed indolent lymphoma to diffuse large B-cell lymphoma; [IC-COMP] OR
2) Classic follicular lymphoma; [IC-COMP] OR
3) Marginal zone lymphoma; [IC-COMP] AND

b) Patient has received at least two lines of systemic therapy; [IC-COMP] AND

B) Patient is ≥ 18 years of age; [IC-COMP] AND

C) Patient has received or plans to receive lymphodepleting chemotherapy prior to infusion of Breyanzi; [IC-COMP] AND

D) Patient has not been previously treated with CAR-T therapy. [IC-COMP]
Note: Examples of CAR-T therapy include Breyanzi, Kymriah® (tisagenlecleucel suspension for intravenous infusion), Tecartus™ (brexucabtagene suspension for intravenous infusion), and Yescarta® (axicabtagene suspension for intravenous infusion).

Dosing. The dose is 50 to 110 x 10^6 CAR-positive viable T-cells administered intravenously as a single dose.[1]

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2. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. ^

Criteria. Approve a single dose if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; [IC-COMP] 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; [IC-COMP] AND

b) Patient has tried a Bruton tyrosine kinase inhibitor; [IC-COMP] 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; [IC-COMP] 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; [IC-COMP] AND

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

1) Patient has disease progression on non-chemoimmunotherapy regimen; OR; [IC-COMP] 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; [IC-COMP] OR

3) Patient has had disease progression on chemoimmunotherapy; [IC-COMP] 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; [IC-COMP] AND

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

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.

SOURCES OF INFORMATION

1. Breyanzi® intravenous infusion [prescribing information]. Bothell, WA: Juno Therapeutics; December 2025.
2. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 1.2026 – December 22, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed January 5, 2026.
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.
6. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). Original effective date 8/7/2019. Implementation date 2/16/2021. Revision date: 07/2025. Accessed February 9, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	03/10/2021
Policy revision	**B-Cell Lymphoma:** Added "or plan to receive" to the requirement that the patient has received lymphodepleting chemotherapy prior to infusion of Breyanzi.	01/14/2022
Policy revision	**B-Cell Lymphoma:** Revised requirement for patients with large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, acquired immunodeficiency syndrome (AIDS)-related DLBCL, and post-transplant lymphoproliferative disorders from having received	08/03/2022

	two or more systemic lines of therapy to having received at least one line of systemic therapy. Added human herpesvirus-8 (HHV8)-positive DLBCL, primary effusion lymphoma and follicular lymphoma, grade 3B to this criterion. Removed gastric mucosa-associated lymphoid tissue (MALT) lymphoma, non-gastric MALT lymphoma, and splenic marginal zone lymphoma from criterion. Revised transformed follicular lymphoma to DLBCL and transformed nodal marginal zone lymphoma to DLBCL to transformed indolent lymphoma to DLBCL.	
Policy revision	Added: "The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy." to the Policy Statement.	07/26/2023
Policy revision	**B-Cell Lymphoma:** Revised acquired immunodeficiency syndrome (AIDS) to human immunodeficiency virus (HIV). Revision based on review of commercial policy revision.	02/22/2024
Policy 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.	06/26/2024
Policy 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.	12/18/2024
Policy revision	No criteria changes. Formatting and notation updates.	03/10/2025
Policy review	No criteria changes. Review based on NCD surveillance review.	06/03/2025
Policy review	No criteria changes. Review based on NCD surveillance review.	09/05/2025
Policy 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".	12/08/2025
Policy revision	**B-Cell Lymphoma:** Added "Marginal zone lymphoma" as one of the conditions for approval after at least two lines of prior systemic therapy.	02/09/2026