Utilization Review Policy 246B

POLICY: Breyanzi Utilization Management Medical Policy

- Breyanzi® (lisocabtagene maraleucel intravenous infusion – Juno Therapeutics)

EFFECTIVE DATE: 6/1/2021
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: UCare Medicare Plans Only (UCare Medicare, EssentiaCare, Group Plans, MSHO, Connect + Medicare, UCare Your Choice)

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.
- 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 2.2024 – April 30, 2024) 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 3.2024 – March 26, 2024) 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]
- **Pediatric Aggressive Mature B-Cell Lymphomas** (version 1.2024 – April 8, 2024) 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] Breyanzi is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Breyanzi REMS.

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 References 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 Reference 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 also covered (and, if applicable, further detailed/referenced) in the corresponding Commercial Care Continuum (CC) Policy. Note: Additional criteria requirements for coverage of the same indication as outlined in the Commercial CC Policy and this Medicare Advantage CC Policy may NOT be the same.

Indications noted with eviCore are managed by eviCore healthcare for those clients who use eviCore for oncology and/or oncology-related reviews. For these indications, a prior authorization should be initiated through eviCore at www.eviCore.com.

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. ^ *eviCore*

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; 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

B) Patient is ≥ 18 years of age; 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.
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. ^ *eviCore*

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; AND

B) Patient meets BOTH of the following (i and ii):

i. Patient has received 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).

ii. Patient has received Venclexta (venetoclax tablets); 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).

Dosing. The dose is 50 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; May 2024.
2. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 4, 2024.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 3, 2024. Search term: lisocabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2024 – April 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 4, 2024.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2024 – March 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 4, 2024.
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. Accessed June 26, 2024.

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 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.	08/03/2022
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
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024