

Medicare Advantage Medical Utilization Review Policy

Policy:	Oncology (Injectable – CAR-T) – Breyanzi Utilization Management Medical Policy <ul style="list-style-type: none"> Breyanzi® (lisocabtagene maraleucel intravenous infusion – Juno Therapeutics)
Date:	07/26/2023
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	All States

OVERVIEW

Breyanzi, a CD19-directed genetically modified autologous T-cell immunotherapy, is indicated for the treatment of adults with **large B-cell lymphoma** 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, 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.¹

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 $\leq -130^{\circ}\text{C}$. The dose of Breyanzi is 50 to 110 x 10⁶ 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.

Guidelines

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

- **B-Cell Lymphomas** (version 5.2022 – July 12, 2022) 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, acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma, and post-transplant lymphoproliferative disorders. Breyanzi can also be used as third-line and subsequent therapy for transformed indolent lymphoma to DLBCL.
- **Pediatric Aggressive Mature B-Cell Lymphomas** (version 3.2022 – October 19, 2022) 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) and neurologic toxicities.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.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

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), or (9)]:

(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) Acquired immunodeficiency syndrome (AIDS)-related diffuse large B-cell lymphoma;
OR



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- (7) Human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma; OR
 - (8) Primary effusion lymphoma; OR
 - (9) Post-transplant lymphoproliferative disorders; 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 transformed indolent lymphoma to diffuse large B-cell 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 10⁶ CAR-positive viable T-cells administered intravenously as a single dose.¹

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 2022.
2. The NCCN B-Cell Lymphoma Clinical Practice Guidelines in Oncology (version 5.2022 – July 12, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed January 17, 2023.
3. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 17, 2023. Search term: lisocabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2022 – October 19, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed January 17, 2023.
5. 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 July 26, 2023.

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	08/03/2022



	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

