Drug Coverage Policy

Effective Date.....2/15/2025
Coverage Policy Number.....IP0130
Policy Title..... Breyanzi

Oncology (Injectable – CAR-T) – Breyanzi

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

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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.

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.

Medical Necessity Criteria

Breyanzi is considered medically necessary when ONE of the following criteria are met (1 or 2):

FDA-Approved Indication

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 plan 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.

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 BOTH of the following (a and b):

a) 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).

b) Patient has received Venclexta (venetoclax tablets); OR

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 del(17p)/TP53 mutation positive disease; OR
(2) Patient is chemotherapy refractory; OR
(3) Patient is unable to receive 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 50 to 110 x 10^6 CAR-positive viable T-cells administered intravenously as a single dose.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	**Description**
38225	Chimeric antigen receptor T-cell therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day (Code effective 1/01/2025)
38226	Chimeric antigen receptor T-cell therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage) (Code effective 1/01/2025)
38227	Chimeric antigen receptor T-cell therapy; receipt and preparation of CAR-T cells for administration (Code effective 1/01/2025)
38228	Chimeric antigen receptor T-cell therapy; CAR-T cell administration, autologous (Code effective 1/01/2025)
0537T	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day (Code effective until 12/31/2024)
0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage) (Code effective until 12/31/2024)
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration (Code effective until 12/31/2024)
0540T	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous (Code effective until 12/31/2024)

HCPCS Codes	**Description**

Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-cd19 car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

***Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.**

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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Lisocabtagene maraleucel" to "Oncology (Injectable – CAR-T) – Breyanzi." **B-Cell Lymphoma: Revised** acquired immunodeficiency syndrome (AIDS) to human immunodeficiency virus (HIV). **Removed** criteria requiring both anti-CD20 monoclonal antibody and an anthracycline-containing chemotherapy regimen for systemic therapy. **Removed** the criteria necessitating an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2 and the absence of primary central nervous system lymphoma. **Removed** the requirement for prescription by or in consultation with a hematologist. **Conditions Not Covered: Removed** criterion regarding exclusion of repeat administration of Breyanzi.	08/01/2024
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.	9/1/2024

	Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: Added new condition of approval.	
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. **Updated CPT Coding:** **Updated:** 0537T, 0538T, 0539T, 0540T to reflect that codes are effective until 12/31/2024 **Added:** 38225, 38226, 38227, 38228 (Codes effective 1/01/2025)	12/15/2025

The policy effective date is in force until updated or retired.