PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Injectable – CAR-T) – Breyanzi Prior Authorization Policy
- Breyanzi® (lisocabtagene maraleucel intravenous infusion – Juno Therapeutics)

REVIEW DATE: 11/13/2024

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 3.2024 – August 26, 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 1.2025 – October 1, 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] 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 2.2024 – September 3, 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 prescription benefit coverage of Breyanzi. All approvals are provided for the duration noted below. 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.

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.

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 3.2024 – August 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 6, 2024.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on November 6, 2024. Search term: lisocabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2024 – September 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 6, 2024.
5. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2025 – October 1, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed November 6, 2024.