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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 12, 2021
Subject:	Breyanzi	**Page:**	1 of 5

Last Review Date: March 8, 2024

Breyanzi

Description

Breyanzi (lisocabtagene maraleucel)

Background
Breyanzi (lisocabtagene maraleucel) is a genetically-modified autologous T cell immunotherapy indicated for the treatment of adult patients with large B-cell lymphoma. Breyanzi is a customized treatment created using an individual patient's own T cells, a type of white blood cell known as a lymphocyte. The patient's T cells are collected and sent to a manufacturing site where they are genetically-modified to include a gene that contains a specific protein (the anti-CD19 CAR transgene) that directs the T-cells to target and kill lymphoma cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells (1).

Regulatory Status
FDA-approved indications: Breyanzi is a CD19-directed genetically-modified autologous T cell immunotherapy indicated for the treatment of adult patients with 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, who have:

- 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 (HSCT) due to comorbidities or age
- relapsed or refractory disease after two or more lines of systemic therapy (1).

Limitations of Use: (1)
Breyanzi is not indicated for the treatment of patients with primary central nervous system (CNS) lymphoma.

Breyanzi has a boxed warning for cytokine release syndrome (CRS) and neurological toxicities. Patients with an active infection or inflammatory disorders should not receive Breyanzi and monitoring for neurological events should be done after treatment with Breyanzi (1).

Breyanzi is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Breyanzi REMS. Healthcare facilities that dispense and administer Breyanzi must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab (Actemra), and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within 2 hours after Breyanzi infusion, if needed for treatment of CRS (1).

Serious infections, including life-threatening or fatal infections, occurred in patients after Breyanzi infusion. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing (1).

CD19-directed CAR-T cell therapy is supported by the National Comprehensive Cancer Network (NCCN) Guidelines for the treatment of B-cell lymphomas only after two or more chemoimmunotherapy regimens and if not previously given (2).

The safety and effectiveness of Breyanzi have not been established in pediatric patients (1).

Related policies
Kymriah, Tecartus, Yescarta

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Breyanzi may be considered **medically necessary** if the conditions indicated below are met.

Breyanzi may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Large B-cell lymphoma (LBCL)
2. Diffuse large B-cell lymphoma (DLBCL)
3. High grade B-cell lymphoma
4. Primary mediastinal large B-cell lymphoma
5. Follicular lymphoma grade 3B

AND ONE of the following:

a. Refractory to first line chemoimmunotherapy
b. Relapsed within 12 months of first-line chemoimmunotherapy
c. Relapsed after first-line chemoimmunotherapy and ineligible for hematopoietic stem cell transplantation (HSCT)
d. Relapsed or refractory after TWO or more lines of systemic therapy including:
    i. Anti-CD20 monoclonal antibody for CD20-positive tumor
    ii. Anthracycline-containing chemotherapy regimen
    iii. Transformed follicular lymphoma **ONLY**: prior chemotherapy for follicular lymphoma and subsequently had chemorefractory disease after transformation to diffuse large B-cell lymphoma

AND ALL of the following:

a. **NO** diagnosis of primary central nervous system (CNS) lymphoma
b. Absence of active infection (including TB, HBV, HCV, and HIV)
c. Patient has adequate organ and bone marrow function as determined by the prescriber
d. Patient is not at risk for HBV infection **OR** patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated
e. Prescriber agrees to monitor the patient for signs and symptoms of cytokine release syndrome (CRS) and administer tocilizumab (Actemra) if needed

f. Prescriber agrees to monitor the patient for signs and symptoms of neurological toxicities
g. Administered in a healthcare facility enrolled in the Breyanzi REMS program
h. **NO** prior therapy with any other gene therapy (e.g., Abecma, Kymriah, Tecartus, Yescarta)
i. **NO** dual therapy with any other gene therapy (e.g., Abecma, Kymriah, Tecartus, Yescarta)

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity One infusion (only one PA approval for one infusion per lifetime)

Rationale

Summary

Breyanzi (lisocabtagene maraleucel) is a CD19-directed genetically-modified autologous cell immunotherapy as a defined composition to reduce variability in CD8-positive and CD4-positive T cell dose. CAR binding to CD19 expressed on the cell surface of tumor and normal B cells induces activation and proliferation of CAR T cells, release of pro-inflammatory cytokines, and cytotoxic killing of target cells. The safety and effectiveness of Breyanzi have not been established in pediatric patients (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Breyanzi while maintaining optimal therapeutic outcomes.

References

1. Breyanzi [package insert]. Bothell, WA: Bristol-Myers Squibb.; January 2024.
2. NCCN Drugs & Biologics Compendium® Lisocabtagene maraleucel 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

Policy History

Date	Action
March 2021	Addition to PA
April 2021	Revised no prior therapy and no dual therapy statements to include any other gene therapy
June 2021	Annual review and reference update
September 2021	Annual review and reference update
March 2022	Annual review and reference update. Per FEP, removed requirement for prior stem cell transplantation and added requirement that patient has adequate organ and bone marrow function as determined by the prescriber. Also added requirement “Transformed follicular lymphoma ONLY: prior chemotherapy for follicular lymphoma and subsequently had chemorefractory disease after transformation to diffuse large B-cell lymphoma”
July 2022	Addition of indications: patients with disease refractory to first-line chemoimmunotherapy or patient has relapsed within 12 months of first-line therapy, or refractory to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy are not eligible for HSCT
September 2022	Annual review and reference update
October 2022	Per FEP, removed duration from PA
December 2022	Annual review
March 2023	Annual review and reference update
September 2023	Annual review and reference update
December 2023	Annual review and reference update
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.