Cell Therapy 360™

Prior Authorization (PA) Submission Tip Sheet for Breyanzi®

1. Locate Payer-Specific Coverage Policy and PA Form

Important Considerations:

- Commercial or MA plans typically require a PA for CAR T cell therapy
- Specific PA requirements may vary among payer coverage policies
- Most payer policies are expected to be published within 3 to 6 months after FDA approval; however, some payers may take up to 12 months
- In the absence of a published coverage policy, PA submissions might be reviewed on a case-by-case basis

Available Resources:

- Insurance coverage look-up tool at CellTherapy360.com
- PA assistance offered by Cell Therapy 360® Patient Support

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; or
  - 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; or
  - relapsed or refractory disease after two or more lines of systemic therapy.

Limitations of Use: BREYANZI is not indicated for the treatment of patients with primary central nervous system lymphoma.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, AND SECONDARY HEMATOLOGICAL MALIGNANCIES

- **Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving BREYANZI. Do not administer BREYANZI to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab with or without corticosteroids.**
- **Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving BREYANZI, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with BREYANZI. Provide supportive care and/or corticosteroids as needed.**
- **T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including BREYANZI.**
- **BREYANZI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS.**

This information is provided for educational purposes only. BMS cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care, and is subject to frequent change. It is the sole responsibility of the healthcare provider to ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

CAR=chimeric antigen receptor; FDA=US Food and Drug Administration; MA=Medicare Advantage.

Please see additional Important Safety Information on pages 4-7 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

PA Submission Tip Sheet for Breyanzi® (cont'd)

2. Gather Required Information

Important Considerations:

- Payer coverage policies typically require detailed PA documentation for CAR T cell therapies, for example:

Diagnosis	LBCL subtype (DLBCL, PMBCL, high-grade BCL, FL3B)
Disease progression	Relapsed or refractory disease
Prior line(s) of therapy	Prior treatment regimen(s) including systemic therapies and/or HSCT
Prior line(s) of therapy	Absence of primary CNS lymphoma
Tumor expression	CD19 test results
Performance status	ECOG performance status score
Organ function	Adequate bone marrow, renal, liver, and/or cardiac function

Available Resources:

- Patient's medical record (eg, chart notes, lab reports)

SELECT IMPORTANT SAFETY INFORMATION

Cytokine Release Syndrome

Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred following treatment with BREYANZI. In clinical trials of BREYANZI, which enrolled a total of 702 patients with non-Hodgkin lymphoma (NHL), CRS occurred in 54% of patients, including ≥ Grade 3 CRS in 3.2% of patients. The median time to onset was 5 days (range: 1 to 63 days). CRS resolved in 98% of patients with a median duration of 5 days (range: 1 to 37 days). One patient had fatal CRS and 5 patients had ongoing CRS at the time of death. The most common manifestations of CRS (≥10%) were fever, hypotension, tachycardia, chills, hypoxia, and headache.

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BCL=B-cell lymphoma; CAR=chimeric antigen receptor; CNS=central nervous system; DLBCL=diffuse large B-cell lymphoma; ECOG=Eastern Cooperative Oncology Group; FL3B=follicular lymphoma grade 3B; HSCT=hematopoietic stem cell transplant; LBCL=large B-cell lymphoma; PA=prior authorization; PMBCL=primary mediastinal large B-cell lymphoma.

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PA Submission Tip Sheet for Breyanzi® (cont'd)

3. Submit PA With Documentation of Medical Necessity for Breyanzi

Important Considerations:

- PA requirements for CAR T cell therapy are typically based on FDA-approved labeling, NCCN® compendia listing, and the eligibility criteria used in registrational clinical trial(s)
- For information regarding the registrational clinical trials, please refer to Breyanzi Prescribing Information
- A letter of medical necessity may be helpful if the PA form is not specific for Breyanzi or when additional information is needed to document medical necessity

Available Resources:

- Breyanzi Prescribing Information
- Applicable NCCN Guidelines®
- Template letters of medical necessity and appeal at CellTherapy360.com

Contact Cell Therapy 360® Patient Support at 1-888-805-4555 for PA support

The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb makes no guarantee regarding reimbursement for any service or item.

SELECT IMPORTANT SAFETY INFORMATION

Cytokine Release Syndrome (cont'd)

Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, diffuse alveolar damage, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS).

Ensure that 2 doses of tocilizumab are available prior to infusion of BREYANZI.

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- **T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including BREYANZI.**
- **BREYANZI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS.**

Cytokine Release Syndrome

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Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, diffuse alveolar damage, renal insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS).

Ensure that 2 doses of tocilizumab are available prior to infusion of BREYANZI.

Neurologic Toxicities

Neurologic toxicities that were fatal or life-threatening, including immune effector cell-associated neurotoxicity syndrome (ICANS), occurred following treatment with BREYANZI. Serious events including cerebral edema and seizures occurred with BREYANZI. Fatal and serious cases of leukoencephalopathy, some attributable to fludarabine, also occurred.

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IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicities (cont'd)

In clinical trials of BREYANZI, CAR T cell-associated neurologic toxicities occurred in 31% of patients, including ≥ Grade 3 cases in 10% of patients. The median time to onset of neurotoxicity was 8 days (range: 1 to 63 days). Neurologic toxicities resolved in 88% of patients with a median duration of 7 days (range: 1 to 119 days). Of patients developing neurotoxicity, 82% also developed CRS.

The most common neurologic toxicities (≥5%) included encephalopathy, tremor, aphasia, headache, dizziness, and delirium.

CRS and Neurologic Toxicities Monitoring

Monitor patients daily for at least 7 days following BREYANZI infusion at a REMS-certified healthcare facility for signs and symptoms of CRS and neurologic toxicities and assess for other causes of neurological symptoms. Monitor patients for signs and symptoms of CRS and neurologic toxicities for at least 4 weeks after infusion and treat promptly. At the first sign of CRS, institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids as indicated. Manage neurologic toxicity with supportive care and/or corticosteroid as needed. Counsel patients to seek immediate medical attention should signs or symptoms of CRS or neurologic toxicity occur at any time.

BREYANZI REMS

Because of the risk of CRS and neurologic toxicities, BREYANZI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS. The required components of the BREYANZI REMS are:

- 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.
- Ensure that a minimum of 2 doses of tocilizumab are available for each patient for infusion within 2 hours after BREYANZI infusion, if needed for treatment of CRS.

Further information is available at www.BreyanziREMS.com, or contact Bristol-Myers Squibb at 1-866-340-7332.

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of BREYANZI. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO).

Serious Infections

Severe infections, including life-threatening or fatal infections, have occurred in patients after BREYANZI infusion. In clinical trials of BREYANZI, infections of any grade occurred in 34% of patients, with Grade 3 or higher infections occurring in 12% of all patients. Grade 3 or higher infections with an unspecified pathogen occurred in 7%, bacterial infections in 3.7%, viral infections in 2%, and fungal infections in 0.7% of patients. One patient who received 4 prior lines of therapy developed a fatal case of John Cunningham (JC) virus progressive multifocal leukoencephalopathy 4 months after treatment with BREYANZI. One patient who received 3 prior lines of therapy developed a fatal case of cryptococcal meningoencephalitis 35 days after treatment with BREYANZI.

Febrile neutropenia developed after BREYANZI infusion in 8% of patients. Febrile neutropenia may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

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IMPORTANT SAFETY INFORMATION (cont'd)

Serious Infections (cont'd)

Monitor patients for signs and symptoms of infection before and after BREYANZI administration and treat appropriately. Administer prophylactic antimicrobials according to standard institutional guidelines. Avoid administration of BREYANZI in patients with clinically significant, active systemic infections.

Viral reactivation: 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. In clinical trials of BREYANZI, 35 of 38 patients with a prior history of HBV were treated with concurrent antiviral suppressive therapy. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing. In patients with prior history of HBV, consider concurrent antiviral suppressive therapy to prevent HBV reactivation per standard guidelines.

Prolonged Cytopenias

Patients may exhibit cytopenias not resolved for several weeks following lymphodepleting chemotherapy and BREYANZI infusion. In clinical trials of BREYANZI, Grade 3 or higher cytopenias persisted at Day 29 following BREYANZI infusion in 35% of patients, and included thrombocytopenia in 25%, neutropenia in 22%, and anemia in 6% of patients. Monitor complete blood counts prior to and after BREYANZI administration.

Hypogammaglobulinemia

B-cell aplasia and hypogammaglobulinemia can occur in patients receiving BREYANZI. In clinical trials of BREYANZI, hypogammaglobulinemia was reported as an adverse reaction in 10% of patients. Hypogammaglobulinemia, either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion, was reported in 30% of patients. Monitor immunoglobulin levels after treatment with BREYANZI and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement as clinically indicated.

Live vaccines: The safety of immunization with live viral vaccines during or following BREYANZI treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during BREYANZI treatment, and until immune recovery following treatment with BREYANZI.

Secondary Malignancies

Patients treated with BREYANZI may develop secondary malignancies. T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including BREYANZI. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes. Monitor lifelong for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing.

Effects on Ability to Drive and Use Machines

Due to the potential for neurologic events, including altered mental status or seizures, patients receiving BREYANZI are at risk for developing altered or decreased consciousness or impaired coordination in the 8 weeks following BREYANZI administration. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, for at least 8 weeks.

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IMPORTANT SAFETY INFORMATION (cont'd)

Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome (IEC-HS)

Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome (IEC-HS), including fatal or life-threatening reactions, occurred following treatment with BREYANZI. IEC-HS is a life-threatening condition with a high mortality rate if not recognized and treated early. Treatment of IEC-HS should be administered per current practice guidelines.

Adverse Reactions

The most common adverse reaction(s) (incidence ≥30%) in:

- LBCL are fever, cytokine release syndrome, fatigue, musculoskeletal pain, and nausea. The most common Grade 3-4 laboratory abnormalities include lymphocyte count decrease, neutrophil count decrease, platelet count decrease, and hemoglobin decrease.

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