Cell Therapy 360™

Prior Authorization (PA) Submission Tip Sheet for Breyanzi®

1. Locate Payer-specific Coverage Policy and PA Form

Important Considerations:

- Commercial or Medicare Advantage plans typically require PA for CAR T cell therapy[1]
- Specific PA requirements may vary among payer coverage policies
- Most payer coverage policies are expected to be published within 3 to 6 months after FDA approval; however, some payers may take up to 12 months[1]
- 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

Indication

BREYANZI is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory (R/R) large B-cell lymphoma after two or more lines of systemic therapy, 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.

Limitation 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 and NEUROLOGIC TOXICITIES

- **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.**
- **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.

Please see Important Safety Information on pages 4-6 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,[1] for example:

Diagnosis	LBCL subtype (DLBCL, PMBCL, high-grade BCL, FL3B)
Disease progression	Relapsed or refractory disease
Prior treatment	Prior lines of systemic therapy (at least 2); patients may have received HSCT
CNS involvement	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 (CRS)

CRS, including fatal or life-threatening reactions, occurred following treatment with BREYANZI. CRS occurred in 46% (122/268) of patients receiving BREYANZI, including ≥ Grade 3 (Lee grading system) CRS in 4% (11/268) of patients. One patient had fatal CRS and 2 had ongoing CRS at time of death. The median time to onset was 5 days (range: 1 to 15 days). CRS resolved in 119 of 122 patients (98%) with a median duration of 5 days (range: 1 to 17 days). Median duration of CRS was 5 days (range: 1 to 30 days) in all patients, including those who died or had CRS ongoing at time of death.

Among patients with CRS, the most common manifestations of CRS include fever (93%), hypotension (49%), tachycardia (39%), chills (28%), and hypoxia (21%). 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.

Sixty-one of 268 (23%) patients received tocilizumab and/or a corticosteroid for CRS after infusion of BREYANZI. Twenty-seven (10%) patients received tocilizumab only, 25 (9%) received tocilizumab and a corticosteroid, and 9 (3%) received corticosteroids only.

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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 and the eligibility criteria used in registrational clinical trial(s)[1]
- For information regarding the registrational clinical trial, please refer to the 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
- Template letters of medical necessity and appeal at CellTherapy360.com

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

Select Important Safety Information

Neurologic Toxicities

Neurologic toxicities that were fatal or life-threatening, occurred following treatment with BREYANZI. CAR T cell-associated neurologic toxicities occurred in 35% (95/268) of patients receiving BREYANZI, including ≥ Grade 3 in 12% (31/268) of patients. Three patients had fatal neurologic toxicity and 7 had ongoing neurologic toxicity at time of death. The median time to onset of the first event was 8 days (range: 1 to 46 days). The onset of all neurologic events occurred within the first 8 weeks following BREYANZI infusion. Neurologic toxicities resolved in 81 of 95 patients (85%) with a median duration of 12 days (range: 1 to 87 days). Three of four patients with ongoing neurologic toxicity at data cutoff had tremor and one subject had encephalopathy. Median duration of neurologic toxicity was 15 days (range: 1 to 785 days) in all patients, including those with ongoing neurologic events at the time of death or at data cutoff.

Seventy-eight (78) of 95 (82%) patients with neurologic toxicity experienced CRS. Neurologic toxicity overlapped with CRS in 57 patients. The onset of neurologic toxicity was after onset of CRS in 30 patients, before CRS onset in 13 patients, same day as CRS onset in 7 patients, and same day as CRS resolution in 7 patients. Neurologic toxicity resolved in three patients before the onset of CRS. Eighteen patients experienced neurologic toxicity after resolution of CRS.

The most common neurologic toxicities included encephalopathy (24%), tremor (14%), aphasia (9%), delirium (7%), headache (7%), dizziness (6%), and ataxia (6%). Serious events including cerebral edema and seizures occurred with BREYANZI. Fatal and serious cases of leukoencephalopathy, some attributable to fludarabine, have occurred in patients treated with BREYANZI.

CAR T= chimeric antigen receptor-modified T cell; 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; PMBCL = primary mediastinal large B-cell lymphoma; R/R = relapsed or refractory.

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- **BREYANZI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS.**

Cytokine Release Syndrome (CRS)

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

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Please see additional Important Safety Information on page 5-6 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

Important Safety Information (cont'd)

Neurologic Toxicities (cont'd)

The most common neurologic toxicities included encephalopathy (24%), tremor (14%), aphasia (9%), delirium (7%), headache (7%) , dizziness (6%), and ataxia (6%). Serious events including cerebral edema and seizures occurred with BREYANZI. Fatal and serious cases of leukoencephalopathy, some attributable to fludarabine, have occurred in patients treated with BREYANZI.

CRS and Neurologic Toxicities Monitoring

Monitor patients daily at a certified healthcare facility during the first week following infusion, for signs and symptoms of CRS and neurologic toxicities. Monitor patients for signs and symptoms of CRS and neurologic toxicities for at least 4 weeks after infusion; evaluate and treat promptly. Counsel patients to seek immediate medical attention should signs or symptoms of CRS or neurologic toxicity occur at any time. At the first sign of CRS, institute treatment with supportive care, tocilizumab or tocilizumab and corticosteroids as indicated.

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.
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer BREYANZI are trained on the management of CRS and neurologic toxicities.

Further information is available at www.BreyanziREMS.com, or contact Bristol-Myers Squibb at 1-888-423-5436.

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. Infections (all grades) occurred in 45% (121/268) of patients. Grade 3 or higher infections occurred in 19% of patients. Grade 3 or higher infections with an unspecified pathogen occurred in 16% of patients, bacterial infections occurred in 5%, and viral and fungal infections occurred in 1.5% and 0.4% of patients, respectively. Monitor patients for signs and symptoms of infection before and after BREYANZI administration and treat appropriately. Administer prophylactic antimicrobials according to standard institutional guidelines.

Febrile neutropenia has been observed in 9% (24/268) of patients after BREYANZI infusion and 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.

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. Ten of the 11 patients in the TRANSCEND study with a prior history of HBV were treated with concurrent antiviral suppressive therapy to prevent HBV reactivation during and after treatment with BREYANZI. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

Please see additional Important Safety Information on page 6 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

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Important Safety Information (cont'd)

Prolonged Cytopenias

Patients may exhibit cytopenias not resolved for several weeks following lymphodepleting chemotherapy and BREYANZI infusion. Grade 3 or higher cytopenias persisted at Day 29 following BREYANZI infusion in 31% (84/268) of patients, and included thrombocytopenia (26%), neutropenia (14%), and anemia (3%). Monitor complete blood counts prior to and after BREYANZI administration.

Hypogammaglobulinemia

B-cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with BREYANZI. The adverse event of hypogammaglobulinemia was reported as an adverse reaction in 14% (37/268) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 21% (56/268) of patients. Hypogammaglobulinemia, either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion, was reported in 32% (85/268) 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. 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 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, during this initial period.

Adverse Reactions

Serious adverse reactions occurred in 46% of patients. The most common nonlaboratory, serious adverse reactions (> 2%) were CRS, encephalopathy, sepsis, febrile neutropenia, aphasia, pneumonia, fever, hypotension, dizziness, and delirium. Fatal adverse reactions occurred in 4% of patients.

The most common nonlaboratory adverse reactions of any grade (≥ 20%) were fatigue, CRS, musculoskeletal pain, nausea, headache, encephalopathy, decreased appetite, diarrhea, hypotension, tachycardia, dizziness, cough, constipation, abdominal pain, vomiting, edema, and infections (pathogen unspecified).

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Reference:

1. Data on file, BMS.

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