Cell Therapy 360™

Breyanzi® Coding & Billing Information

For questions about coding and billing information, call Cell Therapy 360® at 1-888-805-4555

INDICATION

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.

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. Bristol Myers Squibb 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 select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

GLOBAL links to: https://packageinserts.bms.com/pi/pi_breyanzi.pdf

Please see additional Important Safety Information on pages 11-14 and full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

GLOBAL links to: https://packageinserts.bms.com/medguide/medguide_breyanzi.pdf

Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

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.

Breyanzi is for autologous use only and is administered intravenously, as a one-time treatment.[1]* A single dose of Breyanzi contains CAR-positive viable T cells that consist of CD8 and CD4 components, with each component supplied separately in one to four single-dose vials[1]:

- For R/R LBCL after 1 line of therapy, a single dose contains 90 to 110 x 10^6 CAR-positive viable T cells
- For R/R LBCL after ≥2 lines of therapy, a single dose contains 50 to 110 x 10^6 CAR-positive viable T cells

Coding and billing for CAR T cell therapies will vary based on patient's condition, provided services, payer-specific requirements, and selected site/setting of care. Use this guide to review relevant codes and sample claim forms for Breyanzi.

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*This is part of a larger CAR T process that includes apheresis, manufacturing, administration, and monitoring.

CAR=chimeric antigen receptor; CMS=Centers for Medicare & Medicaid Services; CPT=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS=International Classification of Diseases, Tenth Revision, Procedure Coding System; NDC=National Drug Code; R/R LBCL=relapsed or refractory large B-cell lymphoma.

ICD-10-CM Diagnosis Codes

The ICD-10-CM codes listed below for the approved indication for Breyanzi® are provided by Bristol Myers Squibb and should be verified with a patient's payer. Some payers may specify which codes are covered under their policies. Please code to the level of specificity documented in the medical record.

ICD-10-CM Code Range[2]	Description
C82.4_	Follicular lymphoma grade IIIb
C83.3_	Diffuse large B-cell lymphoma
C83.9_	Non-follicular (diffuse) lymphoma, unspecified
C85.1_	Unspecified B-cell lymphoma
C85.2_	Mediastinal (thymic) large B-cell lymphoma
C85.8_	Other specified types of non-Hodgkin lymphoma
Z00.6*	Encounter for examination for normal comparison and control in clinical research program
Z51.12	Encounter for antineoplastic immunotherapy

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.

*This code should be reported only for clinical trial cases. In the event that the CAR T product is purchased in the usual manner but is being used for a clinical trial involving a different product (ie, the clinical trial is for a non-CAR T product), the provider may enter a Billing Note NTE02 ("Diff Prod Clin Trial") on the electronic claim form (or a remark "Diff Prod Clin Trial" on a paper CMS 1450 claim form). Note that Medicare requires all clinical trial claims cases to contain condition code 30 and value code D4 with the 8-digit National Clinical Trial number. To notify Medicare of expanded access use (EAU) of a CAR T product, the provider may enter condition code 90 on the inpatient claim. Effective October 1, 2022, Medicare no longer recognizes Billing Note NTE02 "Expand Acc Use" on the electronic claim 837I (or a remark "Expand Acc Use" on a paper CMS 1450 claim form).[3]

CAR=chimeric antigen receptor; CMS=Centers for Medicare & Medicaid Services; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

For questions about coding and billing information, call Cell Therapy 360® Patient Support at 1-888-805-4555

HCPCS Level II Product Codes

Effective October 1, 2021, Breyanzi® has been assigned a unique Q-code for use in all sites of care and by all payers.[4]

HCPCS Code	Description	Notes for Medicare FFS
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD 19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose	FOR MEDICARE FFS OPPS HOSPITAL CLAIMS AND OTHER PAYER CLAIMS: • 1 billing unit[4]
-JZ	Zero drug amount discarded/not administered to any patient	• Required on all claims for separately payable drugs under Medicare Part B when there is no discarded amount from single-dose containers eligible for payment (effective July 1, 2023)[5]

Effective July 1, 2021, Breyanzi has been assigned a transitional pass-through status under the Medicare FFS OPPS.* Transitional pass-through status is typically granted for up to 3 years.[6]

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.

*Based on OPPS reporting requirements for drugs with a transitional pass-through status, the -TB modifier should be reported for informational purposes when Breyanzi has been acquired under the 340B Drug Pricing Program.[6] Note that effective January 2025, the -TB modifier will be required for all OPPS claims for products acquired under the 340B Drug Pricing Program; the -JG modifier will remain effective only through December 2024. During the course of 2024, hospitals that currently report the -JG modifier may choose to continue use it or choose to transition to the -TB modifier.

CAR=chimeric antigen receptor; FFS=fee for service; HCPCS=Healthcare Common Procedure Coding System; OPPS=Outpatient Prospective Payment System.

NDC Information

Breyanzi® consists of genetically modified autologous T cells, supplied in vials as separate frozen suspensions of each CD8 component and CD4 component.[1] A single dose of Breyanzi contains CAR-positive viable T cells that consist of CD8 and CD4 components, with each component supplied separately in one to four single-dose vials.[1] For R/R LBCL after 1 line of therapy, a single dose contains 90 to 110 x 10^6 CAR-positive viable T cells. For R/R LBCL after ≥2 lines of therapy, a single dose contains 50 to 110 x 10^6 CAR-positive viable T cells.

10-digit Format[1]	11-digit Format	Description
73153-900-01	**73153-0900-01**	Outer carton containing: • Carton for CD8 component, with up to 4 single-dose vials • Carton for CD4 component, with up to 4 single-dose vials

Payers may require that the NDC number is documented on medical claims submitted for provider-administered therapies.

Specific requirements for NDC reporting may vary; however, the 11-digit format is generally preferred for medical claims. Some payers may require reporting the 11-digit NDC number, along with the NDC qualifier, basis of measure, and quantity.[7] For example, the Breyanzi NDC reported in this format would include:

NDC Qualifier	11-digit NDC	Quantity Qualifier	Quantity For a Single Dose
N4	**73153-0900-01**	UN	1

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.

CAR=chimeric antigen receptor; NDC=National Drug Code; R/R LBCL=relapsed or refractory large B-cell lymphoma.

ICD-10-PCS Inpatient Procedure Codes*

Effective for discharges on or after October 1, 2021, the following CAR T designated ICD-10-PCS codes may be reported for inpatient facility services associated with Breyanzi® administration.

ICD-10-PCS Code[8]	Description	Notes for Medicare FFS Under the IPPS†
XW033N7	Introduction of lisocabtagene maraleucel immunotherapy into peripheral vein, percutaneous approach, new technology group 7	For FY 2024: • Assigned to MS-DRG 018 (Chimeric Antigen Receptor [CAR] T cell and Other Immunotherapies), with the average national base payment rate of $257,958 (the exact rate may vary widely based on hospital-specific adjustments)[9,10‡]
XW043N7	Introduction of lisocabtagene maraleucel immunotherapy into central vein, percutaneous approach, new technology group 7	

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.

*Site/setting of care decisions are at the sole discretion of the treating physician.

†For MA patients, billing requirements and reimbursement methodology may vary by plan.

‡The estimated average does not include outlier, NTAP, pass-through payments, or other applicable hospital-specific adjustments.

FFS=fee for service; FY=fiscal year; ICD-10-PCS=International Classification of Diseases, Tenth Revision, Procedure Coding System; IPPS=Inpatient Prospective Payment System; MA=Medicare Advantage; MS-DRG=Medicare Severity Diagnosis Related Group; NTAP=new technology add-on payment.

Hospital Revenue Codes*

The following CAR T designated revenue codes may be reported with accompanying line items billed for services associated with Breyanzi®.

Revenue Code[11]	Description	Notes for Medicare FFS
0871	Cell/gene therapy – cell collection	Charges for services associated with cell collection and cell processing/storage can be reported under 0871, 0872, and 0873, as separate line items for tracking purposes only. Alternatively, these charges can be reported with Breyanzi charges under 0891, as a single line item.[12†‡]
0872	Cell/gene therapy – specialized biologic processing and storage – prior to transport	
0873	Cell/gene therapy – storage and processing after receipt of cells from manufacturer	
0874	Cell/gene therapy – infusion of modified cells	
0891	Pharmacy – specialized processed drugs – FDA-approved cell therapy	

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.

*Site/setting of care decisions are at the sole discretion of the treating physician.

†For Medicare FFS patients, when the charges for collection and preparation of the CAR T cells are included with the charges for the CAR T product (as a single line item under 0891), the reported date of service must be based on the date of CAR T administration. When cell collection and/or cell processing/storage services are initiated and furnished in the hospital outpatient setting, but the CAR T cell therapy is administered in the inpatient setting, all related charges must be reported on the inpatient claim with the date of CAR T administration as the date of service (reported as separate line items for tracking purposes under 0871, 0872, and 0873 or as a single line item along with CAR T product charges under 0891). For more information, please see Chapter 32 of the Medicare Claims Processing Manual.[13]

‡For Medicare FFS patients, a 3-day payment window policy applies to outpatient services furnished by a hospital or an entity wholly owned or wholly operated by the hospital. Note that for IPPS-exempt hospitals, a 1-day payment window applies.[14]

CAR=chimeric antigen receptor; FDA=US Food and Drug Administration; FFS=fee for service; IPPS=Inpatient Prospective Payment System.

CPT® Codes for Outpatient Hospital and Physician Services*

The following CAR T–designated CPT Category III codes may be reported for outpatient hospital facility services or physician services associated with Breyanzi®. Please note that only one of these CPT Category III codes (CPT code 0540T) is separately payable by Medicare under the Hospital OPPS.[15]

CMS has not assigned relative value units or APCs to these Category III CPT codes, with the exception of the CPT code 0540T under the OPPS.[15] As such, they may not be payable by non-Medicare payers.

CPT Category III Code[16]	Description	Hospital Revenue Code†	Medicare FFS Reimbursement Status Under OPPS in CY 2024[15]‡
Apheresis and Preparation			
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	**0871**	Not recognized by OPPS§ (status indicator B)
0538T	Chimeric antigen receptor T cell (CAR T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)	**0872**	
0539T	Chimeric antigen receptor T cell (CAR T) therapy; receipt and preparation of CAR T cells for administration	**0873**	
Administration			
0540T	Chimeric antigen receptor T cell (CAR T) therapy; CAR T cell administration, autologous	**0874**	Paid under APC 5694 (status indicator S, CY 2024 national average payment rate is $323.02)
CMS has instructed MACs that Medicare only covers CAR T therapy when administered in a REMS-certified healthcare facility. When a facility submits a claim, in order to acknowledge that they are REMS-certified, **the claim must have the -KX modifier appended to the CAR T administration code 0540T.** In Transmittal 11179 (released in January 2022), CMS clarified that the -KX modifier is only required for CAR T claims submitted by **outpatient hospital facilities** (Part A outpatient claims) and **physician practices** (Part B professional claims).[14,15]¶			

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.

*Site/setting of care decisions are at the sole discretion of the treating physician.

†See previous page for revenue code descriptions.

‡For MA patients, billing requirements and reimbursement methodology may vary by plan.

§CPT Category III codes 0537T, 0538T, and 0539T can be reported for tracking purposes only as non-covered charges. For more information, please see Chapter 32 of the Medicare Claims Processing Manual.[13]

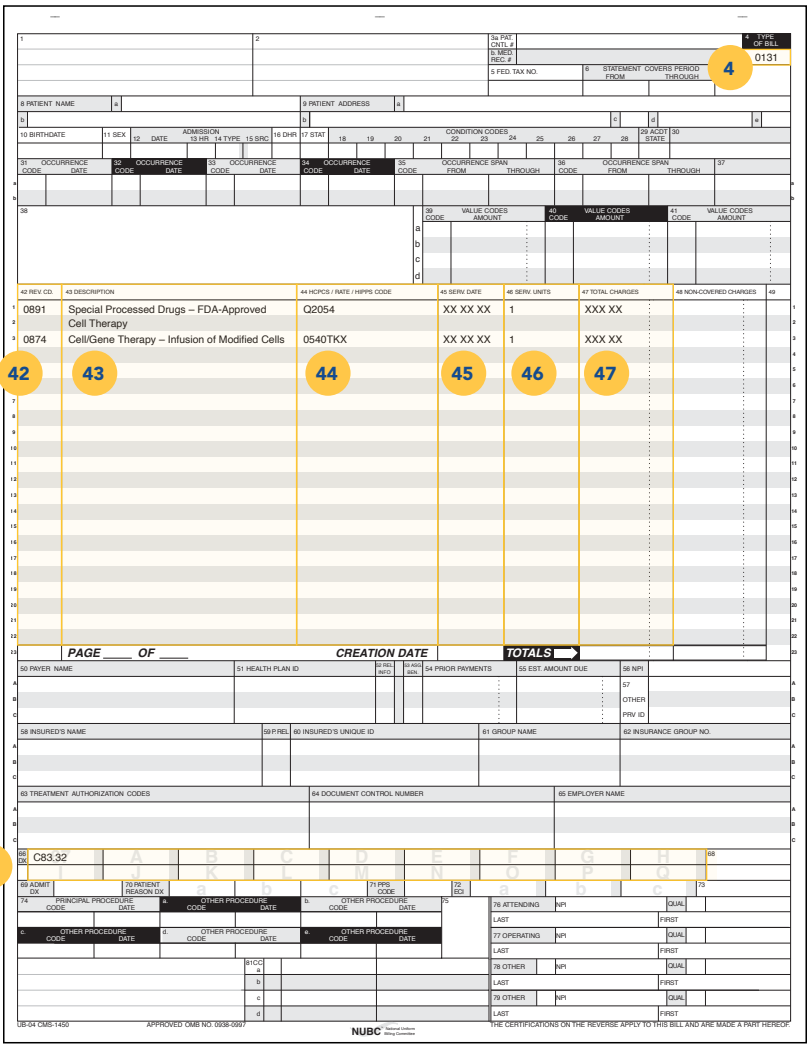
¶Once a hospital facility is identified by a MAC as an FDA REMS-approved facility for a particular CAR T cell therapy, the facility is added to a special edit that allows their inpatient and outpatient facility claims to process automatically regardless of whether the -KX modifier is present on subsequent claims. This special Medicare edit is not applicable to professional claims billing 0540T. For all Medicare professional claims billing this code, the -KX modifier must be present on each CAR T claim.[17]

APC=Ambulatory Payment Classification; CMS=Centers for Medicare & Medicaid Services; CPT=Current Procedural Terminology; CY=calendar year; FDA=US Food and Drug Administration; FFS=fee for service; MA=Medicare Advantage; MAC=Medicare Administrative Contractor; OPPS=Outpatient Prospective Payment System; REMS=Risk Evaluation and Mitigation Strategy.

Please see Important Safety Information on pages 11-14 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

Sample CMS 1450 (UB-04) Claim Form For Outpatient Hospital Facilities[18]



4 **FL 4:** Enter the appropriate type of bill code. For example[19]:
- 0131 for an outpatient hospital facility

42 **FL 42:** Enter the appropriate revenue code for each reported line. For example[11,12]:
- 0874 for CAR T infusion
- 0891 for Breyanzi®

43 **FL 43:** Enter the description for the corresponding revenue code in FL 42.

NOTE: Some payers may require to report drug NDC number(s) in FL 43.

44 **FL 44:** Enter relevant HCPCS Level II and CPT® codes, along with applicable modifiers. For example[3,4,5,13,14,16]:
- 0540T for CAR T infusion and -KX modifier
- Q2054 for Breyanzi and -JZ modifier

45 **FL 45:** Enter corresponding date(s) of service.

46 **FL 46:** Enter appropriate units of service.

NOTE: For Q2054, 1 unit of service is reported per therapeutic dose of Breyanzi.[3]

47 **FL 47:** Enter total charges for each reported line.

67 **FL 67:** Enter appropriate ICD-10-CM diagnosis code(s) for patient condition(s). For example[2]:
- C83.32 for diffuse large B-cell lymphoma, intrathoracic lymph nodes

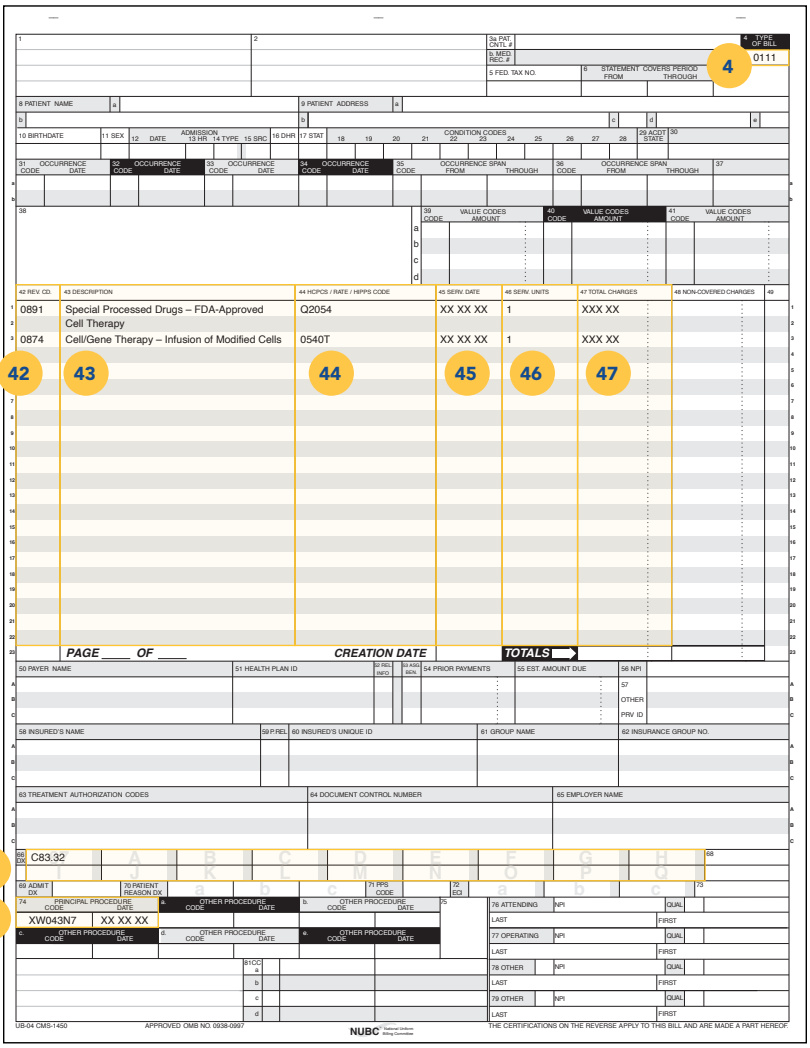
Requirements may vary; refer to specific payer policy*

These sample forms are for informational purposes only. 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.

*Billing instructions have been issued for Medicare FFS patients. For more information, please see Chapter 32 of the Medicare Claims Processing Manual, as well as Medicare Transmittals 11179 and 11774.[13,17,20]

CAR=chimeric antigen receptor; CMS=Centers for Medicare & Medicaid Services; CPT=Current Procedural Terminology; FFS=fee for service; FL=form locator; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; NDC=National Drug Code.

Sample CMS 1450 (UB-04) Claim Form For Inpatient Hospital Facilities[18]



4 **FL 4:** Enter the appropriate type of bill code. For example[19]:
- 0111 for an inpatient hospital facility

42 **FL 42:** Enter the appropriate revenue code for each reported line. For example[11,12]:
- 0874 for CAR T infusion
- 0891 for Breyanzi®

43 **FL 43:** Enter the description for the corresponding revenue code in FL 42.

NOTE: Some payers may require to report drug NDC number(s) in FL 43.

44 **FL 44:** If required by payer, enter relevant HCPCS Level II code, along with the applicable modifier. For example[4,16]:
- 0540T for CAR T infusion
- Q2054 for Breyanzi

45 **FL 45:** Enter corresponding date(s) of service.

46 **FL 46:** Enter appropriate units of service.

NOTE: For Q2054, 1 unit of service is reported per therapeutic dose of Breyanzi.[3]

47 **FL 47:** Enter total charges for each reported line.

67 **FL 67:** Enter appropriate ICD-10-CM diagnosis code(s) for patient condition(s). For example[2]:
- C83.32 for diffuse large B-cell lymphoma, intrathoracic lymph nodes

74 **FL 74:** Enter relevant ICD-10-PCS procedure code(s) with corresponding date(s) of service. For example for Breyanzi infusion[9]:
- XW033N7 or XW043N7

Requirements may vary; refer to specific payer policy*

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*Billing instructions have been issued for Medicare FFS patients. For more information, please see Chapter 32 of the Medicare Claims Processing Manual, as well as Medicare Transmittals 11179 and 11774.[13,17,20]

CAR=chimeric antigen receptor; CMS=Centers for Medicare & Medicaid Services; FFS=fee for service; FL=form locator; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS=International Classification of Diseases, Tenth Revision, Procedure Coding System; NDC=National Drug Code.

INDICATION

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.

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.**

Cytokine Release Syndrome

Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred following treatment with BREYANZI. Among patients receiving BREYANZI for LBCL (N=418), CRS occurred in 46% (190/418), including ≥ Grade 3 CRS in 3.1% of patients. In patients receiving BREYANZI after two or more lines of therapy for LBCL, CRS occurred in 46% (122/268), including ≥ Grade 3 CRS in 4.1% 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 98% with a median duration of 5 days (range: 1 to 17 days). In patients receiving BREYANZI after one line of therapy for LBCL, CRS occurred in 45% (68/150), including Grade 3 CRS in 1.3% of patients. The median time to onset was 4 days (range: 1 to 63 days). CRS resolved in all patients with a median duration of 4 days (range: 1 to 16 days).

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Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

IMPORTANT SAFETY INFORMATION (cont'd)

Cytokine Release Syndrome (cont'd)

The most common manifestations of CRS (≥ 10% in LBCL) included fever (94%), hypotension (42%), tachycardia (28%), chills (23%), hypoxia (16%), and headache (12%).

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. Of the patients who received BREYANZI for LBCL (n=418), 23% received tocilizumab and/or a corticosteroid for CRS, including 10% who received tocilizumab only and 2.2% who received corticosteroids only.

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.

In patients receiving BREYANZI after two or more lines of therapy for LBCL, CAR T cell-associated neurologic toxicities occurred in 35% (95/268), including ≥ Grade 3 cases in 12% of patients. Three patients had fatal neurologic toxicity and 7 had ongoing neurologic toxicity at time of death. The median time to onset of neurotoxicity was 8 days (range: 1 to 46 days). Neurologic toxicities resolved in 85% of patients with a median duration of 12 days (range: 1 to 87 days). In patients receiving BREYANZI after one line of therapy for LBCL, CAR T cell-associated neurologic toxicities occurred in 27% (41/150) of patients, including Grade 3 cases in 7% of patients. The median time to onset of neurologic toxicity was 8 days (range: 1 to 63 days). The median duration of neurologic toxicity was 6 days (range: 1 to 119 days). In all patients combined receiving BREYANZI for LBCL, CAR T cell-associated neurologic toxicities occurred in 33% (136/418), including ≥ Grade 3 cases in 10% of patients. The median time to onset was 8 days (range: 1 to 63), with 87% of cases developing by 16 days. Neurologic toxicities resolved in 85% of patients with a median duration of 11 days (range: 1 to 119 days). Of patients developing neurotoxicity, 77% (105/136) also developed CRS.

The most common neurologic toxicities (≥ 5% in LBCL) included encephalopathy (20%), tremor (13%), aphasia (8%), headache (6%), dizziness (6%), and delirium (5%).

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.

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Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

IMPORTANT SAFETY INFORMATION (cont'd)

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 patients receiving BREYANZI for LBCL from 3 clinical studies, infections of any grade occurred in 36%, 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 4.3%, viral infections in 1.9% and fungal infections in 0.5%.

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.

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 patients who received BREYANZI for LBCL, 15 of 16 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. Grade 3 or higher cytopenias persisted at Day 29 following BREYANZI infusion for LBCL in 36% of patients, and included thrombocytopenia in 28%, neutropenia in 21% and anemia in 6%. Monitor complete blood counts prior to and after BREYANZI administration.

Please see additional Important Safety Information on pages 11-14 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

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IMPORTANT SAFETY INFORMATION (cont'd)

Hypogammaglobulinemia

B-cell aplasia and hypogammaglobulinemia can occur in patients receiving BREYANZI. In patients receiving BREYANZI for LBCL, hypogammaglobulinemia was reported as an adverse reaction in 11% of patients. Hypogammaglobulinemia, either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion, was reported in 28% 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.

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 nonlaboratory adverse reactions (incidence ≥ 30%) in LBCL are fever, CRS, fatigue, musculoskeletal pain, and nausea. The most common Grade 3-4 laboratory abnormalities (≥ 30%) in LBCL include lymphocyte count decrease, neutrophil count decrease, platelet count decrease, and hemoglobin decrease.

Please see additional Important Safety Information on pages 11-14 and full Prescribing Information, including Boxed WARNINGS and Medication Guide.

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