

Breyanzi® (lisocabtagene maraleucel) (Intravenous)

Document Number: MH-0590

Last Review Date: 10/22/2021

Date of Origin: 03/01/2021

Dates Reviewed: 03/2021, 07/2021, 10/2021, 11/2021

Customization Dates: 04/01/2022

Effective Dates: 04/01/2022

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I. Length of Authorization

Coverage will be provided for one treatment course (1 dose of Breyanzi) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 1 carton (1 to 4 vials) of up to 110 million autologous anti-cd19 CAR-positive viable T-cells

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit (1 infusion of up to 110 million autologous anti-cd19 CAR-positive viable T-cells)

III. Initial Approval Criteria ¹⁻⁷

Coverage is provided in the following conditions:

Submission of medical records (chart notes) related to the medical necessity criteria is **REQUIRED** on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

- Patient is at least 18 years of age; **AND**
- Patient does not have a clinically significant active systemic infection or inflammatory disorder; **AND**

- Patient has not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy, and will not receive live vaccines during lisocabtagene maraleucel treatment and until immune recovery following treatment; **AND**
- Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
- Prophylaxis for infection will be followed according to standard institutional guidelines; **AND**
- Healthcare facility has enrolled in the BREYANZI REMS Program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; **AND**
- Patient has not received prior CAR-T therapy; **AND**
- Patient has not received prior anti-CD19 therapy, (e.g., tafasitamab, etc.) OR patient previously received anti-CD19 therapy and re-biopsy indicates CD-19 positive disease; **AND**
- Used as single agent therapy (not applicable to lymphodepleting or additional chemotherapy while awaiting manufacture); **AND**
- Patient does not have primary central nervous system lymphoma; **AND**

B-Cell Lymphomas † ‡ ◻^{1,2,7,8}

- Patient has diffuse large B cell lymphoma (DLBCL), high-grade B-cell lymphoma, primary mediastinal B-cell lymphoma (PMBCL), follicular lymphoma grade 3B, AIDS-related B-cell lymphoma (e.g., diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma, not otherwise specified), or monomorphic post-transplant lymphoproliferative disorder (B-cell type); **AND**
 - Used as additional therapy for patients with intention to proceed to transplant who have a partial response following second-line therapy for relapsed or refractory disease; **OR**
 - Used for treatment of disease that is in second or greater relapse; **OR**
- Patient has histologic transformation of follicular lymphoma, gastric or non-gastric MALT lymphoma, or nodal or splenic marginal zone lymphoma to DLBCL OR Richter's transformation of CLL to DLBCL; **AND**
 - Patient received at least two (2) prior lines of chemoimmunotherapy which must have included an anthracycline or anthracenedione-based regimen, unless contraindicated

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); ◻ Orphan Drug

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration ¹

Indication	Dose
B-Cell Lymphomas	<p><u>Lymphodepleting chemotherapy:</u></p> <ul style="list-style-type: none">Administer cyclophosphamide 300 mg/m² and fludarabine 30 mg/m² intravenously daily for three days. <p><u>Breyanzi infusion:</u></p> <ul style="list-style-type: none">Infuse 2 to 7 days after completion of lymphodepleting chemotherapy.A single dose of Breyanzi contains 50 to 110 × 10⁶ CAR-positive viable T cells (consisting of 1:1 CAR-positive viable T cells of the CD8 and CD4 components), with each component supplied separately in one to four single-dose vials.
<p>For autologous use only. For intravenous use only.</p> <ul style="list-style-type: none">Breyanzi is prepared from the patient's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure.One treatment course consists of lymphodepleting chemotherapy followed by a single infusion of Breyanzi.Confirm Breyanzi availability prior to starting the lymphodepleting regimen.Confirm the patient's identity with the patient identifiers on the shipper and the respective Certificate of Release for Infusion (RFI Certificate) prior to infusion.Delay the infusion of BREYANZI if the patient has unresolved serious adverse events from preceding chemotherapies, active uncontrolled infection, or active graft-versus-host disease (GVHD).	
<p><u>Premedication:</u></p> <ul style="list-style-type: none">Premedicate with 650 mg acetaminophen and 25-50 mg diphenhydramine (or another H1-antihistamine) 30-60 minutes prior to infusion. Avoid prophylactic system corticosteroids which may interfere with Breyanzi activity.	
<p><u>Monitoring after infusion:</u></p> <ul style="list-style-type: none">Monitor patients daily at a certified healthcare facility during the first week following infusion for signs and symptoms of CRS and neurologic toxicities.Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.Instruct patients to refrain from driving or hazardous activities for 8 weeks following infusion.	
<ul style="list-style-type: none">Store infusion bag in the vapor phase of liquid nitrogen (less than or equal to minus 130°C). Thaw prior to infusion.In case of manufacturing failure, a second manufacturing may be attempted.Additional chemotherapy (not the lymphodepletion) may be necessary while the patient awaits the product.Ensure that 2 doses of tocilizumab and emergency equipment are available prior to infusion and during the recovery period.Breyanzi contains human blood cells that are genetically modified with replication incompetent self-inactivating lentiviral vector. Follow universal precautions and local biosafety guidelines for handling and disposal.	

VI. Billing Code/Availability Information

HCPCS Code:

- Q2054 – Lisocabtagene maraleucel, up to 110 million autologous anti-cd19 car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

NDC:

- Breyanzi suspension for intravenous infusion [Each vial contains between 6.9×10^6 and 322×10^6 CAR-positive viable T cells in 4.6 mL cell suspension (between 1.5×10^6 and 70×10^6 CAR-positive viable T cells/mL)]: 73153-0900-xx

VII. References

1. Breyanzi [package insert]. Bothell, WA; Juno Therap., Inc., February 2021. Accessed October 2021.
2. Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. *Lancet*. 2020 Sep 19;396(10254):839-852. doi: 10.1016/S0140-6736(20)31366-0. Epub 2020 Sep 1.
3. Mejstrikova E, Hrusak O, Borowitz MJ, et al. CD19-negative relapse of pediatric B-cell precursor acute lymphoblastic leukemia following blinatumomab treatment. *Blood Cancer J*. 20177; 659. DOI 10.1038/s41408-017-0023-x
4. Ruella M, Maus MV. Catch me if you can: Leukemia Escape after CD19-Directed T Cell Immunotherapies. *Computational and Structural Biotechnology Journal* 14 (2016) 357–362.
5. Braig F, Brandt A, Goebeler M, et al. Resistance to anti-CD19/CD3 BiTE in acute lymphoblastic leukemia may be mediated by disrupted CD19 membrane trafficking. *Blood*; 129:1, 2017 Jan.
6. Majzner RG, Mackall CL. Tumor Antigen Escape from CAR T-cell Therapy. *Cancer Discov* 2018;8:1219-1226.
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) lisocabtagene maraleucel. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2021.
8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2022. National Comprehensive Cancer Network, 2021. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed October 2021.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site

C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C83.90	Non-follicular (diffuse) lymphoma, unspecified site
C83.91	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified intrapelvic lymph nodes

C83.97	Non-follicular (diffuse) lymphoma, unspecified spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified extranodal and solid organ sites
C85.10	Unspecified B-cell lymphoma, unspecified site
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17	Unspecified B-cell lymphoma, spleen
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region of lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Article and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC