Breyanzi® (lisocabtagene maraleucel)
(Intravenous)

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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]

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. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **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 other anti-CD19 therapy (e.g., tafasitamab, blinatumomab, loncastuximab tesirine, etc.) OR patient previously received other anti-CD19 therapy and re-biopsy indicates CD-19 positive disease; **AND**
- Used as single agent therapy (not applicable to lymphodepleting or bridging chemotherapy while awaiting manufacture); **AND**
- Patient does not have primary central nervous system lymphoma; **AND**

B-Cell Lymphomas † ‡ Φ [1,2,7-12]

- Patient has diffuse large B cell lymphoma (DLBCL), high-grade B-cell lymphoma, primary mediastinal B-cell lymphoma (PMBCL), follicular lymphoma (FL) grade 3b, HIV-related B-cell lymphoma (i.e., HIV-related DLBCL, primary effusion lymphoma, and HHV8-positive DLBCL, not otherwise specified), or monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type); **AND**
    - Used for primary refractory disease (partial response, no response, or progression) or relapsed disease within 12 months after completion of first-line therapy; **OR**
    - Used for relapsed or refractory disease after first-line chemoimmunotherapy in patients NOT eligible for hematopoietic stem cell transplantation (HSCT) *(Note: Excludes HIV-related B-cell lymphoma and monomorphic PTLD)*; **OR**
    - Used as second-line therapy for relapsed or refractory disease >12 months after completion of first-line therapy if no intention to proceed to transplant; **OR**
    - Used as additional therapy for relapsed or refractory disease >12 months after completion of first-line therapy and a partial response following second-line therapy *(Note: For DLBCL, FL grade 3b, or PMBCL, patient must also have no intention to proceed to transplant)*; **OR**
    - Used for relapsed or refractory disease after two (2) or more lines of systemic therapy; **OR**
- Patient has Richter's transformation of CLL to DLBCL; **AND**
    - Patient received at least two (2) prior lines of chemoimmunotherapy for indolent or transformed disease which must have included an anthracycline or anthracenedione-based regimen, unless contraindicated; **OR**
- Patient has histologic transformation of an indolent lymphoma (follicular lymphoma or marginal zone lymphoma) to DLBCL; **AND**
    - Disease is refractory to first-line chemoimmunotherapy or has relapsed within 12 months of first-line chemoimmunotherapy; **AND**

- Patient is a candidate for autologous hematopoietic stem cell transplant (HSCT); **OR**

- Disease is relapsed or refractory after first-line chemoimmunotherapy and patient is NOT eligible for HSCT; **OR**
- Patient received at least two (2) prior lines of chemoimmunotherapy for indolent or transformed disease which must have included an anthracycline or anthracenedione-based regimen, unless contraindicated

Pediatric Aggressive Mature B-Cell Lymphomas ‡ [1,2,7,11,12]

- Patient is ≤ 18 years of age; **AND**
- Patient has primary mediastinal large B-Cell lymphoma; **AND**
- Used as consolidation or additional therapy in patients with a partial response after therapy for relapsed or refractory disease; **AND**
- Patient has previously received ≥ 2 prior chemoimmunotherapy regimens

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage cannot be renewed.

V. Dosage/Administration [1]

Indication	Dose
All indications	<u>Lymphodepleting chemotherapy</u>: • Administer cyclophosphamide 300 mg/m² and fludarabine 30 mg/m² intravenously daily for three days. <u>Breyanzi infusion for relapsed/refractory disease after receiving at least ONE line of therapy:</u> • Infuse 2 to 7 days after completion of lymphodepleting chemotherapy. • A single dose of Breyanzi contains 90 to 110 × 10^6 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. <u>Breyanzi infusion for relapsed/refractory disease after receiving at least TWO lines of therapy:</u> • Infuse 2 to 7 days after completion of lymphodepleting chemotherapy. • A single dose of Breyanzi contains 50 to 110 × 10^6 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.
For autologous use only. For intravenous use only. • Breyanzi is prepared from the patient's T-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).
Premedication: • 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. **Monitoring after infusion**: • 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.
• 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 bridging 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 x 10^6 CAR-positive viable T cells in 4.6 mL cell suspension (between 1.5×10^6 and 70 x 10^6 CAR-positive viable T cells/mL)]: 73153-0900-xx

VII. References

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8. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2023. National Comprehensive Cancer Network, 2023. 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 2023.
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12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Aggressive Mature B-Cell Lymphomas Version 1.2023 National Comprehensive Cancer Network, 2023. 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 2023.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
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 Articles (LCAs), 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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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