



MEDICAL COVERAGE POLICY

SERVICE: Lisocabtagene Maraleucel (Breyanzi®)

Policy Number: 291

Effective Date: 1/1/2024

Last Review: 10/09/2023

Next Review: 10/09/2024

Important note: Unless otherwise indicated, medical policies will apply to all lines of business.

Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.

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PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to [Medicare NCD 110.24 Chimeric Antigen Receptor \(CAR\) T-cell Therapy](#)

For Medicaid plans, please confirm coverage as outlined in the [Texas Medicaid Provider Procedures Manual | TMHP](#) (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

BSWHP may consider lisocabtagene maraleucel (Breyanzi®) medically necessary for the treatment of large B-cell lymphoma when ALL of the following criteria are met:

1. The member has a diagnosis of large B-cell lymphoma [i.e. 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] ; **AND**
 2. Member is \geq 18 years old; **AND**
 3. Member diagnosed by a hematologist or oncologist; **AND**
 4. Member has documentation of CD19 tumor expression; **AND**
 5. One-time, single administration treatment; **AND**
 6. Member will be using lisocabtagene maraleucel at a certified treatment center; **AND**
 7. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
 8. Member has adequate bone marrow, renal, hepatic, pulmonary, and cardiac function; **AND**
 9. Member has one of the following:
 - a. Relapsed or refractory disease after two or more prior lines of systemic therapy
 - b. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy
 - c. 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
- AND**



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10. Member has or will receive lymphodepleting chemotherapy (fludarabine 30 mg/m² IV daily and cyclophosphamide 300 mg/m² IV daily) for 3 days before infusion of lisocabtagene maraleucel; **AND**
11. Member will NOT be treated with more than 110 x 10⁶ viable CAR-T cells; **AND**
12. Member does NOT have any of the following conditions:
 - a. Primary central nervous system (CNS) lymphoma
 - b. Active hepatitis B (HBs AG-positive), active hepatitis C, uncontrolled infection, or HIV infection
 - c. History of CNS disorders (ex. seizure disorder, cerebrovascular ischemia)
 - d. History of any autoimmune disease requiring systemic immunosuppression**AND**
13. The individual has NOT previously been treated with CD-19 targeted therapy or prior CD-19 targeted CAR-T cell therapy; **AND**
14. Member has been assessed by a hematologist/oncologist to be an appropriate candidate for apheresis.

BSWHP considers repeat administration of lisocabtagene maraleucel experimental and investigational because the effectiveness of this strategy has not been established.

BSWHP considers lisocabtagene maraleucel to be experimental and investigational for all other indications.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:

Chimeric antigen receptor (CAR) T cells and genetically engineered T-cell receptor (TCR T) cells are manufactured by collecting lymphocytes from a patient or donor and modifying them using gene transfer techniques. Viral vectors are introduced that express cell receptors that are highly specific for tumor antigens. CAR T and TCR T cells are then infused back into the patient where they direct a targeted immune response to cancerous tissue. CAR T cells express a hybrid receptor with an extracellular single-chain antibody fragment, a transmembrane domain, and at least 1 intracellular signaling domain. CAR T cells are most often used to treat hematological malignancies, and a common target is B-cell cluster of differentiation antigen 19 (CD19).

The U. S. Food and Drug Administration (FDA) granted approval for lisocabtagene maraleucel (Breyanzi®) on February 5, 2021 for the treatment of adult patients with relapsed or refractory 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. The boxed warning includes the clarification that lisocabtagene maraleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risk of cytokine release syndrome (CRS) and neurological toxicities.



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The FDA approval of lisocabtagene maraleucel is based on data from the TRANSCEND (NCT02631044) open-label, multicenter, single-arm Phase I trial involving 299 patients, 204 receiving treatment in the intended dose range, of whom 192 were evaluable for efficacy. Results showed that 54% of those taking lisocabtagene maraleucel had a complete response, with another 19% having a partial response. Among the complete responders, 65% had remission lasting at least 6 months and 62% had remission lasting at least 9 months. With respect to safety, the most common grade 3 or higher adverse effects were neutropenia (76%) and thrombocytopenia (39%). Serious adverse reactions occurred in 46% of patients.

The FDA updated approval of lisocabtagene maraleucel to include treatment for adult patients with relapsed or refractory LBCL after first-line chemoimmunotherapy based on an randomized, open-label, multicenter trial (TRANSFORM; NCT03575351). The estimated 1-year event free survival was 45% in the lisocabtagene maraleucel arm and 24% in the standard therapy arm. 66% of lisocabtagene maraleucel arm achieved complete response vs 39% in the standard therapy arm.

Lisocabtagene maraleucel was evaluated in a single-arm, open-label, multicenter trial (PILOT; NCT03483103) in transplant-ineligible patients with relapsed or refractory LBCL after one line of chemoimmunotherapy. Overall response rate was 80% with lisocabtagene maraleucel with 54% complete response.

CODES:

Important note: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes:	0540T - Chimeric antigen receptor T cell (CAR-T) therapy; CAR-T cell administration, autologous 96409 - Chemotherapy administration; intravenous, push technique, single or initial substance/drug 96413 - Chemotherapy administration; intravenous infusion technique; up to 1 hour, single or initial substance/drug
HCPCS Codes:	Q2054 Lisocabtagene maraleucel, up to 110 million autologous anti-cd19 car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
ICD10 codes:	C82.40 - C82.59 Follicular lymphoma C83.30 - C83.39 Diffuse large B-cell lymphoma C83.90 - C83.99 Non-follicular (diffuse) lymphoma C85.20 - C85.29 Mediastinal (thymic) large B-cell lymphoma
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	04/22/2021	New policy



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Updated	05/27/2021	Removed Oncology Analytics line, added apheresis criteria
Updated	07/22/2021	Added clinician reviewer criteria
Updated	06/23/2022	Added NCD information
Updated	10/27/2022	Removed language with CMS LCD since NCD applies. Updated HCPCS code. Added new criteria for relapsed/refractory disease after first-line chemoimmunotherapy. Removed Texas Mandate HB1584 language from main policy section as the policy is compliant. Minor formatting update.
Reviewed	10/09/2023	Applied new layout and format.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Almásbak H, Aarvak T, Vemuri MC. CAR T cell therapy: a game changer in cancer treatment. *J Immunol Res.* 2016;2016:5474602.
2. Brentjens RJ. Are chimeric antigen receptor T cells ready for prime time? *Clin Adv Hematol Oncol.* 2016;14(1):17-19.
3. Brudno JN, Somerville RP, Shi V, et al. Allogeneic T cells that express an anti-CD19 chimeric antigen receptor induce remissions of B-cell malignancies that progress after allogeneic hematopoietic stem-cell transplantation without causing graft-versus-host disease. *J Clin Oncol.* 2016;34(10):1112-1121.
4. Children’s Hospital of Philadelphia (CHOP). What to Expect: CAR T-cell Therapy Process. 2017. Available at: <http://www.chop.edu/centers-programs/cancer-immunotherapy-program/your-experience>. Accessed August 8, 2017.
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12. Leukemia and Lymphoma Society (LLS). Chimeric Antigen Receptor (CAR) T-Cell Therapy. 2017. Available at: <https://www.lls.org/treatment/types-of-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy>.



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14. Lymphoma Research Foundation (LRF). Diffuse Large B-Cell Lymphoma (DLBCL). 2016. Available at: <http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300153>. Accessed August 8, 2017.
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16. Prescribing Label: Breyanzi (lisocabtagene maraleucel) suspension for intravenous infusion injection, for intravenous use. Bristol-Myers Squibb Company. Available at: <http://www.accessdata.fda.gov>. Accessed October 2022.
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Note:

Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSA.