MEDICAL COVERAGE POLICY **SERVICE: Lisocabtagene Maraleucel (Breyanzi®)**	
Policy Number:	**291**
Effective Date:	**12/01/2021**
Last Review:	**10/27/2022**
Next Review Date:	**10/27/2023**

Important note
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Lisocabtagene Maraleucel (Breyanzi®)

PRIOR AUTHORIZATION: Required

POLICY:

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination).

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM. Texas Mandate HB1584 is applicable for Medicaid plans.

Lisocabtagene Maraleucel (Breyanzi®)

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 ≥ 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

10. Member has or will receive lymphodepleting chemotherapy (fludarabine 30 mg/m^2 IV daily and cyclophosphamide 300 mg/m^2 IV daily) for 3 days before infusion of liscabtagene maraleucel; **AND**
11. Member will NOT be treated with more than 110 x 10^6 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.

OVERVIEW

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.

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:
CODES: 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
CPT Not Covered:	
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:	

CMS: NCD 110.24 - Chimeric Antigen Receptor (CAR) T-cell Therapy: Medicare covers autologous treatment for cancer with T-cells expressing at least one chimeric antigen receptor (CAR) when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies (REMS) and used for a medically accepted indication as defined at Social Security Act section 1861(t)(2) -i.e., is used for either an FDA-approved indication (according to the FDA-approved label for that product), or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia.
Effective date: 08/07/2019. Implementation date: 09/20/2021

POLICY HISTORY:

Status	Date	Action
New	04/22/2021	New policy
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.

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 may modify it at a later date 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.

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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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