Diffuse large B-cell lymphoma (DLBCL) is derived from white blood cells that grow in an uncontrolled, rapid manner and therefore require treatment (LLS, 2021). DLBCL is the most common type of non-Hodgkin lymphoma accounting for approximately 25% of NHL cases and approximately 7 per 100,000 people in the United States is diagnosed with DLBCL annually (UpToDate 2021). Although 5-year survival rates in the first-line setting range from 60% to 70%, up to 50% of patients become refractory to or relapse after treatment (Crump et al. 2017). In eligible patients, high-dose immunotherapy followed by autologous stem-cell transplantation (ASCT) has been the standard of care for relapsed-refractory DLBCL (R/R DLBCL). However, >60% of patients are ineligible for a transplant, and more than half of those undergoing ASCT will subsequently relapse. First-line treatment for DLBCL is based on the combination of the anti-CD20 monoclonal antibody rituximab with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy (WHO, 2016). The addition of rituximab to CHOP significantly improved treatment outcomes, but 30% to 40% of patients are still not cured (ESMO, 2018). CAR T-cell therapy offers an additional option for patients with DLBCL. CAR T-cells are a form of immunotherapy in which immune cells are genetically engineered to target an antigen present on tumor cells so that they seek out those cells specifically; these T-cells then initiate an active and sustained immune response against the target cells (Skrabek, P et al. 2019).

Breyanzi (lisocabtagene maraleucel; liso-cel) is indicated for the treatment of adult patients with R/R LBCL after two or more lines of systemic therapy, including 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. Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma. Breyanzi is a CD19-directed genetically modified autologous cell immunotherapy. The product is administered using a defined ratio of CD4-positive and CD8-positive CAR T cells to reduce variability in CD8-positive and CD4-positive T cell dose. A single dose contains 50 to 110 x 10^6 CAR-positive viable T cells (consisting of 1:1 CAR-positive viable T cells of the CD8 and CD4 components). Breyanzi is the fourth CAR T-cell therapy to receive FDA approval, and the third gene therapy approved for certain types of non-Hodgkin lymphoma, including DLBCL. DLBCL is the most common type of non-Hodgkin lymphoma in adults.

Previous CAR T-cell approvals include Kymriah (tisagenleleucel) for the treatment of R/R LBCL in adults or R/R B-cell acute lymphoblastic leukemia; Yescarta (axicabtagene ciloleucel) for the treatment of R/R LBCL; Tecartus (brexucabtagene autoleucel) for the treatment of adults with R/R mantle cell lymphoma. Kymriah, Yescarta and Breyanzi are indicated for R/R LBCL after two or more lines of systemic therapy.
**COVERAGE POLICY**

Breyanzi (liso-cel) for treatment of relapsed or refractory large B-cell lymphomas (R/R LBCL) **may be considered medically necessary** when **ALL** of the following clinical criteria are met:

1. Histologically confirmed diagnosis of CD19-positive large B-cell lymphoma (by testing or analysis confirming CD19 protein on the surface of the B-cell) of **ONE** of the following types:
   a. Diffuse large B-cell lymphoma (DLBCL), not otherwise specified; OR
   b. Transformed DLBCL from indolent histology; OR
   c. High-grade B-cell lymphoma (HGBL); OR
   d. Primary mediastinal large B-cell lymphoma (PMBCL or PMBL); OR
   e. Follicular lymphoma Grade 3B
   **NOTE:** Breyanzi is not indicated for the treatment of patients with primary CNS lymphoma

2. Relapsed or refractory disease, defined as progression after **TWO** or more lines of systemic therapy (which may or may not include therapy supported by autologous cell transplant), including **ALL** of the following
   a. Anti-CD20 monoclonal antibody for CD20-positive tumor (e.g., rituximab)
   **AND**
   b. An anthracycline-containing chemotherapy regimen (e.g., doxorubicin); OR
   For transformed follicular lymphoma: Prior chemotherapy for follicular lymphoma with chemotherapy refractory disease after transformation to DLBCL
   **AND**

3. Eastern Cooperative Oncology Group Performance Status (ECOG-PS) of 0 or 1; **AND**
   **Informational Note:** Clinical trials excluded patients who are ECOG PS ≥ 2, have CNS involvement, or have serious infections and patients must have adequate organ and marrow function. The TRANSCEND study initially allowed individuals with an ECOG score of 2 to enroll, but for unknown reasons, 2 years after study initiation (2017), the protocol was amended to restrict to ECOG of 0 to 1. A total of 4 patients (1% of study population) had ECOG of 2.

4. Adequate bone marrow, cardiac, pulmonary, and organ function with no deterioration expected within 4 weeks after Breyanzi infusion, as determined by the treating oncologist/hematologist. Lab results must be submitted within 14 days of authorization confirming that member has adequate organ and bone marrow function; **AND**

5. Clinical notes from member’s medical records, including: All relevant history and physical exams, disease staging, all prior therapies and cancer treatment history, anticipated treatment course applicable, labs and/or tests supporting the diagnosis (lab results must be dated within 14 days of request); **AND**

6. Confirmation/attestation of **ALL** of the following:
   a. Member will not receive ANY of the following:
      o A G-CSF agent within the first 3 weeks after Breyanzi infusion or until CRS has resolved; **AND**
      **Informational Note:** 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 in 31% (84/268) of patients, and included thrombocytopenia (26%), neutropenia (14%), and anemia (3%).
      o Live virus vaccine for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during Breyanzi treatment and **until immune recovery** following treatment with Breyanzi.
      **AND**
   b. For members with a history of allogeneic stem cell transplant: Documentation (e.g., recent chart notes) confirming that member has no signs of active graft versus host disease (GVHD); **AND**
   c. Member has not received, or is being considered for CAR-T therapy, other gene therapy or investigational cellular therapy for cancer; **AND**
   d. For women of reproductive potential:
      o Member is not pregnant or breast-feeding: Negative serum pregnancy test within the past 30 days; **AND**
      o Member has been counseled on the use of effective contraception during treatment.
CONTINUATION OF THERAPY
The safety and efficacy of repeat treatment has not been studied and is currently not supported by any compendia nor indicated in the current FDA approved labeling. Requests for reauthorization or beyond one dose is considered not medically necessary and will not be authorized.

Repeat administration of CAR-T cell is experimental and investigational since the safety and efficacy beyond ONE treatment has not been studied and is not indicated in the current FDA approval for Breyanzi. The evidence is insufficient to determine the effects on net health outcomes.

LIMITATIONS AND EXCLUSIONS
There are no contraindications listed in the manufacturer’s labeling at this time. The following are considered exclusions based on insufficient evidence:
1. Prior treatment, or being considered for treatment, with CAR-T therapy or other gene therapy; OR repeat treatment Breyanzi
2. Pregnancy: Not recommended for women who are pregnant, and pregnancy after Breyanzi infusion should be discussed with the treating physician
   Informational Note: It is not known if Breyanzi has the potential to be transferred to the fetus. Based on the mechanism of action, if the transduced cells cross the placenta, they may cause fetal toxicity, including B-cell lymphocytopenia and hypogammaglobulinemia.
3. Active hepatitis B virus (HBsAG positive) or active hepatitis C virus (anti-HCV positive) if viral load is detectable; Human immunodeficiency virus (HIV) positive. NOTE: A history of hepatitis B or hepatitis C is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing.
4. Active, uncontrolled infections (fungal, bacterial, viral, or other uncontrolled infections); Uncontrolled or requires IV antimicrobials (antibiotics, antifungals, antiprotozoals, antivirals).
5. Active inflammatory disorders
6. Active GVHD
7. Autoimmune disease requiring systemic immunosuppression
8. Presence or history of:
   a. Active or primary CNS disease; detectable cerebrospinal fluid malignant cells or brain metastases
   b. Primary CNS lymphoma or CNS disorder such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement
   [Informational Note: NCCN guidelines define CNS involvement (CNS leukemia CNS-3) as the following: WBC count of ≥ 5 leukocytes/mcL in the CSF with the presence of lymphoblasts]
9. Progressive vascular tumor invasion, thrombosis, or embolism
10. Venous thrombosis or embolism not managed on a stable regimen of anticoagulation

The following are considered experimental, investigational and unproven based on insufficient evidence:
1. Any indications other than those listed above (including primary CNS lymphoma)
   Based on the peer-reviewed medical literature the safety and effectiveness for indications other than the medically necessary indication listed above has not been established.
2. Prior treatment with any form of CAR T-cell therapy, or repeat administration of Breyanzi

DURATION OF APPROVAL: Duration sufficient for ONE single course of treatment.

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, an oncologist/hematologist at a certified treatment center

AGE RESTRICTIONS: 18 years of age or older at time of infusion
Pediatric patients: The safety and efficacy of Breyanzi in patients under 18 years of age have not been established.

DOSSING CONSIDERATIONS: A treatment course consists of lymphodepleting chemotherapy (consists of fludarabine 30 mg/m²/day and cyclophosphamide 300 mg/m²/day concurrently for 3 days) followed by Breyanzi (liso-cel) 2 to 7 days after completion of lymphodepleting chemotherapy. Confirm availability of autologous liso-cel prior to initiating lymphodepleting chemotherapy; AND
Breyanzi (IV infusion only): For autologous use only, administer 2-7 days after completing lymphodepleting chemotherapy; for \(50 \text{ to } 110 \times 10^6\) CAR-positive viable T cells (consisting of 1:1 CD8 and CD4 components) IV. Actual cell counts and volumes for infusion are on the release for infusion (RFI) certificates. 

*Informational Note: Dose based on the number of CAR-positive viable T-cells per vial. A single dose contains 50-110 \(x \times 10^6\) CAR-positive viable T-cells. The CD8 and CD4 components are supplied in separate vials; more than 1 vial of each component may be required for a complete dose.*

Premedication (acetaminophen and diphenhydramine) is required prior to liso-cel infusion. Ensure tocilizumab and emergency equipment are available prior to infusion and during recovery period.

**MONITORING PARAMETERS:**
- Monitor for signs/symptoms of Cytokine Release Syndrome (CRS), Neurologic Toxicities [BOXED WARNINGS]
- Screen for hepatitis B virus (HBV), hepatitis C virus, and HIV in accordance with clinical guidelines prior to collection of cells for manufacturing. Monitor CBC prior to and after liso-cel administration.
- The American Society of Clinical Oncology HBV screening and management provisional clinical opinion (ASCO [Hwang 2020]) recommends HBV screening with hepatitis B surface antigen, hepatitis B core antibody, total Ig or IgG, and antibody to hepatitis B surface antigen prior to beginning (or at the beginning of) systemic anticancer therapy; do not delay treatment for screening/results. Detection of chronic or past HBV infection requires a risk assessment to determine antiviral prophylaxis requirements, monitoring, and follow-up.

**QUANTITY LIMITATIONS:**
ONE (1) single treatment course of Breyanzi per lifetime; AND

Concurrent Authorizations: Authorizations for Breyanzi will also receive approval of Actemra (tocilizumab). Max 8 single dose vials per lifetime [Refer to Actemra (tocilizumab) Policy No: C10265-A].

*Informational Note: Actemra is indicated for the treatment of CAR T cell-induced severe or life-threatening CRS in patients \(\geq 2\) years of age. According to the FDA approved labeling for intravenous tocilizumab, the dose should not exceed 800 mg per infusion every 4 weeks for RA or CRS patients (Actemra Prescribing Information, 2020).*

**ADMINISTRATION:**
1. Breyanzi is considered a provider-administered therapy under the expertise and safety measures available in certified treatment centers enrolled in the REMS program
   - 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.
   - Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer Breyanzi are trained on the management of CRS and neurologic toxicities.

**DOCUMENTATION REQUIREMENTS.** Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.
DRUG INFORMATION

ROUTE OF ADMINISTRATION: Intravenous Infusion

DRUG CLASS: Antineoplastic Agent, Anti-CD19; Antineoplastic Agent, Chimeric Antigen Receptor (CAR) T Immunotherapy; CAR-T Cell Immunotherapy; Cellular Immunotherapy, Autologous.

FDA-APPROVED USES: Large B-cell lymphoma, relapsed or refractory Treatment of relapsed or refractory large B-cell lymphoma in adults after ≥2 lines of systemic therapy, including 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. FDA Approval: February 5, 2021.

Limitations of use: Not indicated for the treatment of primary central nervous system (CNS) lymphoma

COMPELILARY APPROVED OFF-LABEL USES: None

RISK EVALUATION AND MITIGATION STRATEGY (REMS): Available only through the BREYANZI REMS due to the serious risks of CRS and neurologic toxicities.

BOXED WARNING: CRS; Neurologic Toxicities

SUMMARY OF MEDICAL EVIDENCE

The FDA based its approval of Breyanzi on data from the TRANSCEND NHL 001 phase 1 trial of 268 patients with R/R LBCL; 192 patients (n=192) were treated with Breyanzi.

- Primary outcome measures included treatment-related adverse events, dose-limiting toxicities and objective response rate. Key secondary outcome measures included complete response rate, duration of response and progression-free survival.
- Of treated patients, 73% achieved a response, including 54% who had minimal or no detectable lymphoma remaining following treatment (complete remission, or CR).
- Of 104 patients treated with Breyanzi who achieved a best overall response of CR, 65% had remission lasting at least 6 months and 62% had remission lasting at least nine months.

TRANSCEND NHL 001. An open-label, multicenter, pivotal Phase 1 study that assessed the efficacy and safety of Breyanzi in patients (n=269) with R/R LBCL after at least 2 lines of therapy (Abramson et al., 2020).

- Patient population included adult patients [the average age was 63 years (range, 54-70)] with relapsed or refractory large B-cell lymphomas.; a broad range of histological subgroups were included: DLBCL, high-grade B-cell lymphoma with rearrangements of MYC and either BCL2, BCL6, or both (double-hit or triple-hit lymphoma), diffuse large B-cell lymphoma transformed from any indolent lymphoma, primary mediastinal B-cell lymphoma, and follicular lymphoma grade 3B.
- Breyanzi was administered in both inpatient and outpatient.
- Primary endpoints were the incidence of treatment-related adverse events (AEs), the probability of dose-limiting toxicities (DLTs), and the objective response rate (ORR), defined as the proportion of patients who achieved a best overall response of complete response or partial response.
- Key secondary endpoints were the proportion of patients achieving a complete response (CR), the duration of response (DOR), progression-free survival (PFS), and overall survival (OS).
- Primary and secondary end points were met.
- Overall, 256 patients of 344 total patients who underwent leukapheresis were evaluable for efficacy in the study. According to study results:
  - 192 patients were treated with Breyanzi at a dose of 50 to 110 x 10⁶ CAR-positive viable T cells and were evaluated for efficacy.
Of the treated patients, 73% achieved a response, including 54% with a complete response rate (patient had minimal or no detectable lymphoma remaining following treatment) and 19% who achieved a partial response.

Of the 104 patients who achieved complete response, 65% had remission lasting at least 6 months and 62% had remission lasting at least 9 months.

The median time to first response was 1 month. The median duration of response was 16.7 months in all responders, and patients who achieved a complete response did not reach a median duration of response. The estimated median duration of response among patients with partial response was 1.4 months.

The labeling carries a boxed warning for CRS, which is a systemic response to the activation and proliferation of CAR T cells, causing high fever and flu-like symptoms and neurologic toxicities. Both CRS and neurological events can be life-threatening. Among 269 patients treated with lisocabtagene maraleucel:

- Most frequent treatment-emergent adverse events were neutropenia (n=169; 63%), anemia (n=129; 48%), fatigue (n=119; 44%), CRS (n=113; 42%), and nausea (n=90; 33%)
- Grade 3 or worse CRS was reported in 2% (6) patients. 1 patient had fatal CRS and 2 had ongoing CRS at time of death.
- Neurological events of any grade occurred in 30% (80) patients. Neurological events occurred during or after CRS in 73% (58) patients. Grade 3 or worse neurological events occurred in 10% (27) patients. 3 patients had fatal neurologic toxicity and 7 had ongoing neurologic toxicity at the time of death.
- The most common toxicities included encephalopathy, tremor, aphasia, delirium, headache, ataxia, and dizziness. Neurologic toxicities resolved in 81 of 95 patients, with a median duration of 12 days.
- Serious AEs occurred in 46% of patients; fatal AEs occurred in 4% of patients

Breyanzi was administered and monitored in the outpatient setting to approximately 10% of patients in this trial. The manufacturer is continuing to evaluate the safety of Breyanzi for outpatient administration and monitoring in the phase II TRANSCEND-OUTREACH 007 and TRANSCEND-PILOT-017006 pilot trials.

Post-Marketing Requirement (PMR) study
A PMR study has been required to further assess long-term safety of Breyanzi and the risk of secondary malignancies occurring after treatment. The multicenter, prospective, observational safety study will include at least 1500 adult patients with R/R large B-cell lymphoma after 2 or more lines of systemic therapy. Patients will be followed for 15 years after treatment with Breyanzi. The primary endpoint will be evaluation for secondary malignancy, which will include the collection and analysis of blood and/or biopsy specimens of certain malignancies for evaluation of insertional mutagenesis.

A digital platform, Cell Therapy 360, is provided by the manufacturer (BMS) to support the patient and physician treatment experience. Patients will be able to track production and receive support and other relevant information. The manufacturer will also provide patients with wearable technology to help patients track their temperature in real time.

Comparative Studies
A head-to-head trial and indirect treatment comparison studies evaluating the safety and efficacy of FDA-approved CAR T-cell therapies are lacking. The differences in patient selection (e.g., prior treatment(s) and transplantation status) and trial design (e.g., use of bridging chemotherapy and different CRS grading scales) make comparisons across the therapies a challenge. According to a final evidence report published by ICER, there is insufficient evidence to conclude the superiority of one CAR T therapy over the other for NHL, particularly because the studies of CAR T therapies are all small, single-arm trials with short follow-up. These limiting factors also make the comparative efficacy analyses versus standard therapy markedly difficult (ICER, March 2018).

Although there are no comparative studies, a review of the safety data from the pivotal trial shows Breyanzi with a superior safety profile with lower rates of ≥ 3 grade CRS compared with data reported in the pivotal trials of Kymriah and Yescarta:

- Breyanzi: TRANSCEND NHL-001 trial: 2%
- Kymriah: JULIET trial: 22%
- Yescarta: ZUMA-1 trial: 11%
Breyanzi has notably lower rates of severe CRS and neurotoxicity in the pivotal trial in comparison to Kymriah and Yescarta (though 4 treatment-related deaths occurred) (TRANSCEND-NHL-001).

- Neurologic toxicities occurred in 87% of patients taking Yescarta and 58% of DLBCL patients who were administered Kymriah. Thirty-five percent of patients who received Breyanzi developed neurologic toxicities after administration.

**National and Specialty Organizations**

The use of liso-cel in large B-cell lymphoma has not been addressed in guidelines (March 2021).

**National Comprehensive Cancer Network (NCCN)** has Clinical Practice Guidelines on B-Cell Lymphomas (version 1.2021; January 20, 2021) which include Kymriah and Yescarta as options for adult patients with relapsed or refractory large B-cell lymphoma in accordance with FDA approved labeling.

**American Society of Clinical Oncology (ASCO)** issued a CAR T-Therapy Policy Brief in 2019 supporting coverage of CAR T-cell therapy for all FDA-approved indications.

**National Institute for Health and Care Excellence (NICE)** is developing guidance on the use of lisocabtagene maraleucel for treating large B-cell lymphoma after at least 2 therapies: Lisocabtagene maraleucel for treating relapsed or refractory aggressive B-cell non-Hodgkin lymphoma [ID1444] Expected publication date: September 22, 2021

**SUPPLEMENTAL INFORMATION**

**Chimeric Antigen Receptor T-cells (CAR T-cells):** T-cells that have been genetically altered in order to improve the ability of the T-cells to fight cancer. The genetic modification creates a new and special receptor on the surface of the T-cell. This special receptor is called a CAR and there are many CARs on the surface of the T-cell. CAR enhances the ability of the T-cell to recognize and attach to a specific protein, called an antigen, on the surface of a cancer cell. (CMS)

CAR T-cells are most often used to treat hematological malignancies, and a common target is B-cell cluster of differentiation antigen 19 (CD19). CAR T-cell infusion is typically administered in an outpatient setting, although patients receiving treatment may require an inpatient stay if adverse events are encountered. Patients typically must remain close to the treatment facility or clinic for a period of up to 6-8 weeks for monitoring and rapid identification of treatment-related adverse events that require hospitalization. CAR T therapy is associated with serious complications, including some fatal neurologic events and CRS, which is a severe systemic response (e.g., high fever, flu-like symptoms, hypotension, mental status changes) to the activation and proliferation of CAR T-cells. CRS is observed in nearly all treated patients and may be life-threatening, but it typically responds to treatment with aggressive supportive care that includes tocilizumab and corticosteroids. Neurologic toxicities may also be severe or life-threatening. Other adverse events include hypersensitivity reactions, serious infections, prolonged cytopenias, prolonged hypogammaglobulinemia, and second malignancies.

**Cytokine release syndrome (CRS):** An acute systemic inflammatory response syndrome characterized by fever, with or without multiple organ dysfunction that is associated with CAR-T cell therapy or other forms of immunotherapy. Clinical manifestations include fever, which may be accompanied by fatigue, headache, rash, diarrhea, arthralgia, and myalgia. Milder CRS can progress to a more severe syndrome, which may include hypotension, hypoxia, and uncontrolled systemic inflammatory response with circulatory collapse, vascular leakage, peripheral and/or pulmonary edema, renal failure, cardiac dysfunction, and multiorgan system failure.

**Eastern Cooperative Oncology Group Performance Status (ECOG PS)**

A scale used to determine the individual's level of functioning; standard criteria for measuring how the disease impacts a patient’s daily living abilities:

- **0** Fully active, able to carry on all pre-disease performance without restriction
- **1** Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
- **2** Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
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Next Review Due By: April 2022

3 Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4 Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5 Deceased

The scale was developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group and published in 1982.

Refractory DLBCL: Refers to disease that fails to respond adequately to treatment. Primary refractory DLBCL refers specifically to an inadequate response to initial treatment.

Relapsed DLBCL: Refers to disease that recurs after achievement of a complete response to initial treatment.

CODING & BILLING INFORMATION

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AVAILABLE DOSAGE FORMS: Breyanzi is supplied in vials as separate frozen suspensions of each CD8 and CD4 component; each component is packed in a carton containing up to 4 vials, depending upon the concentration of the cryopreserved drug product CAR-positive vial T cells.

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY


REFERENCES

Government Agency
- NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). Available at: CMS NCD
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ClinicalTrials.gov.

U.S. Food and Drug Administration (FDA)
- U.S. FDA approves Bristol Myers Squibb’s Breyanzi (lisocabtagene maraleucel), a New CAR T Cell Therapy for Adults with Relapsed or Refractory Large B-Cell Lymphoma. [press release]. Bristol Myers Squibb; February 5, 2021.

Prescribing Information and Drug Compendia
Breyanzi (lisocabtagene maraleucel) [prescribing information]. Bothell, WA: Bristol-Myers Squibb Company; February 2021.


Peer Reviewed Publications


National and Specialty Organizations
American Cancer Society

European Society for Medical Oncology (ESMO)


Breyanzi (lisocabtagene maraleucel; liso-cel)

Policy No. 400

Last Approval: 4/5/2021

Next Review Due By: April 2022

Other Peer Reviewed and Professional Organization Publications (used in the development of this policy)


APPENDIX

Reserved for State specific information (to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.

Centers for Medicare & Medicaid Services (CMS)
On August 7th, 2019 CMS published a National Coverage Determination (NCD) regarding CAR-T therapy coverage in the Medicare program. According to the NCD, for services performed on or after August 7, 2019, CMS 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. Reference Publication 100-03, National Coverage Determination (NCD) Manual Section 110.24 for complete coverage criteria. (Rev. 10454, Issued: 11-13-20, Effective: 08-07-19, Implementation: 02-16-21)

NOTE: On 11/2020, a Change Request (CR) was issued to inform of coverage effective for claims with dates of service on or after August 7, 2019 [Link: TN 10454 (Medicare Claims Processing)]