Wellmark Advantage Health Plan

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Effective Date: 08/04/2022

Breyanzi® (lisocabtagene maraleucel)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indications
   b. FDA approved age
   c. Prescribed by on in consultation with an oncologist
   d. Treatment of patients with relapsed or refractory Non-Hodgkin's lymphoma of the following subtypes:
      i. Diffuse large B-cell lymphoma (DLBCL)
      ii. Primary mediastinal B-cell lymphoma (PMBCL)
      iii. Follicular lymphoma, grade 3B
   e. Received ≥ 2 lines of chemotherapy, including rituximab and anthracycline
      OR
   f. Refractory disease or relapse within 12 months of first-line anti-CD20 and anthracycline therapy
      OR
   g. Refractory disease to first-line chemoimmunotherapy or relapse after first-line therapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
   h. Patients must meet all of the following
      i. ECOG performance status of 0 - 2
      ii. Creatinine clearance greater than 30 mL/min
      iii. Alanine aminotransferase less than 5 times the upper limit of normal
      iv. Left ventricular ejection fraction greater than 40%
      v. No known active CNS involvement by primary malignancy (secondary CNS involvement is allowed)
      vi. No history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy
      vii. No infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy
      viii. No HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable
      ix. No presence of graft-vs-host disease (GVHD)
      x. No myocardial infarction, cardiac angioplasty or stenting, unstable angina, or New York Heart Association Class II or greater congestive heart failure events within 6 months
      xi. No thromboembolic events within 6 months

xii. No pulmonary disease requiring oxygen dependence or pulmonary disease such as idiopathic pulmonary fibrosis, organizing pneumonia (eg, bronchiolitis obliterans), drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis per chest computed tomography (CT) scan at screening
xiii. No clinically significant CNS pathology such as epilepsy, seizure, paresis, aphasia, stroke, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis

i. Have not received prior treatment with any CAR-T therapy despite indication or any other genetically-modified T-cell therapy or are being considered for treatment with any other genetically-modified T-cell therapy
j. Only to be administered at certified bone marrow/stem cell transplant centers
k. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the Wellmark Advantage Health Plan utilization management medical drug list
l. The prescriber needs to submit documentation of response to Breyanzi within 3 months following therapy as a follow-up to the prior approval request
m. If new diagnoses are FDA approved, coverage will be determined based on the FDA approved indication on a case by case basis until fully evaluated by the Wellmark Advantage Health Plan Pharmacy and Therapeutics Committee

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months with the allowance of only one dose per lifetime
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- CAR-T therapy is a type of treatment the utilizes the body's own immune system to fight cancer. T-cells are collected from the patient via apheresis and are genetically engineered in the laboratory to produce chimeric antigen receptors on the cell surface, allowing the T-cells to recognize an antigen on target cancer cells. Once the tumor cells are identified, they are attacked and killed by the CAR-T therapy.

- CAR-T therapy has not been studied when given following prior treatment with any CAR-T therapy or following any other genetically-modified T-cell therapy.

- Due to the risk of cytokine release syndrome and neurological toxicities, CAR-T therapies are only allowed to be given at treatment centers certified by their REMS programs. CAR-T REMS programs require certified hospitals and their clinics to have on-site, immediate access to tocilizumab and an understanding of how to manage the risks of the associated CAR-T side effects.

- Breyanzi is indicated 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. Breyanzi is not indicated for the treatment of patients with primary central nervous system lymphoma.

- Safety and efficacy as third-line therapy were established in the TRANSCEND trial, an open-label, multicenter, single-arm study of 268 patients with relapsed or refractory large B-cell non-Hodgkin lymphoma. Subjects must have been treated with an anthracycline and rituximab (or other CD20-targeted agent) and have relapsed or refractory disease after at least 2 lines of systemic therapy or after allogeneic HSCT. For patients who received previous CD19-targeted therapy, CD19-positive lymphoma confirmed on a biopsy had to be confirmed since completing the prior CD19-targeted therapy. Patients were excluded from the study if they had an ECOG performance status of greater than 2, a creatinine clearance less than 30 mL/min, alanine aminotransferase greater than 5 times the upper limit of normal, left ventricular ejection fraction less than 40%, active CNS involvement by primary malignancy, history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy, had active infection, or the presence of graft-vs-host disease. The primary endpoints were complete response (CR) rate and duration of response (DOR). Seventy-three percent of patients achieved a response (95% CI: 67% - 80%), including 54% who experienced complete response (95% CI: 47% - 61%) and 19% who achieved a partial response (95% CI: 14% - 26%). Median duration of response was 16.7 months in all responders (95% CI: 5.3 – not reached (NR)). For patients who achieved a CR, median duration of response was not reached (95% CI: 16.7 – NR). For patients achieving a PR, median duration of response was 1.4 months (95% CI: 1.1 – 2.2). Of 104 patients treated with Breyanzi who achieved a CR, 65% had remission lasting at least six months and 62% had remission lasting at least nine months.

- Safety and efficacy as second-line therapy were established in the TRANSFORM trial, an randomized, open-label, parallel-group, multicenter study of 184 patients with relapsed or refractory large B-cell non-Hodgkin lymphoma. Subjects must have been treated with an anthracycline and rituximab (or other CD20-targeted agent) and have relapsed or refractory disease after first-line therapy. Patients were excluded from the study if they had an ECOG performance status of greater than 1, a creatinine clearance less than 45 mL/min, alanine aminotransferase greater than 5 times the upper limit of normal, left ventricular ejection fraction less than 40%, active CNS involvement by primary malignancy, history of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy, or had active infection. The primary endpoint was event free survival (EFS). Breyanzi significantly improved median EFS compared with standard therapy (10.1 months vs. 2.3 months; HR = 0.34; p-value < 0.0001) and also significantly increased median progression free survival (PFS) (14.8 months vs. 5.7 months; HR = 0.4; p-value = 0.0001). Sixty-six percent of patients assigned Breyanzi achieved complete response to therapy compared with 39% of patients assigned standard treatment (p-value < 0.0001).

- Disease should be measured/staged with PET-CT. Focal uptake in nodal and extranodal sites is considered involvement with lymphoma, including spleen, liver, bone, thyroid, and so on. A measurable node must have a longest diameter (LDi) greater than 1.5 cm. A measurable extranodal lesion should have an LDi greater than 1.0 cm. All other lesions (including nodal, extranodal, and assessable disease) should be followed as nonmeasured disease (eg, cutaneous, GI, bone, spleen, liver, kidneys, pleural or pericardial effusions, ascites).

References:

1. Breyanzi [prescribing information]. Bothell, WA: Bristol Myers Squibb; June 2022.
2. National Comprehensive Cancer Network. B-cell lymphomas (Version 4.2022). 2022 June 9. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on June 28, 2022.
3. Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10; 124 (2): 188 - 195.
4. Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicenter seamless design study. Lancet. 2020 Sep 19; 396 (10254): 839 – 52.
5. Clinicaltrials.gov. A phase 1, multicenter, open-label study of JCAR017, CD19-targeted chimeric antigen receptor (CAR) t-cells, for relapsed and refractory (R/R) b-cell non-hodgkin lymphoma (NHL) (NCT02631044). Available at: https://clinicaltrials.gov/ct2/show/NCT02631044. Accessed on February 8, 2021.

6. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of hodgkin and non-hodgkin lymphoma: the lugano classification. J Clin Oncol. 2014 Sep 20; 32 (27): 3059 – 68.
7. Clinicaltrials.gov. A global randomized multicenter phase 3 trial of JCAR017 compared to standard of care in adult subjects with high-risk, second-line, transplant-eligible relapsed or refractory aggressive b-cell Non-hodgkin lymphomas (TRANSFORM) (NCT03575351). Available at: https://clinicaltrials.gov/ct2/show/NCT03575351. Accessed on May 31, 2022.
8. Amorosi D. Liso-cel significantly improves outcomes in second-line DLBCL. 2021 Dec 11. Available at: https://www.healio.com/news/hematology-oncology/20211211/lisocel-significantly-improves-outcomes-in-secondline-dlbcl. Accessed on May 21, 2022.
9. Healio.com. FDA grants priority review to Breyanzi for second-line treatment of large B-cell lymphoma. 2022 Feb 17. Available at: https://www.healio.com/news/hematology-oncology/20220217/fda-grants-priority-review-to-breyanzi-for-secondline-treatment-of-large-bcell-lymphoma. Accessed on May 31, 2022.
10. U.S. Department of Health and Human Services. Common terminology criteria for adverse events (Version 5.0). 2017 Nov 27. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf. Accessed on July 6, 2022.

Policy History		
#	Date	Change Description
1.3	Effective Date: 08/04/2022	Updated to align criteria across all CAR-T policies and include new indication for use as second-line therapy in DLBCL
1.2	Effective Date: 06/09/2022	Updated to add preliminary criteria for use as second-line therapy in DLBCL
1.1	Effective Date: 04/14/2022	Updated to remove CD19 requirement as NCCN guidelines state CAR-T can work without being positive for CD19 disease
1.0	Effective Date: 01/01/2022	Effective date of policy.

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*