Medicare Advantage Medical Benefit Drug Policy

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Effective Date: 02/10/2022

Yescarta™ (axicabtagene ciloleucel)

HCPCS: Q2041

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 age
   b. Prescribed by or in consultation with an oncologist
   c. 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, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (TFL)
      i. Subjects must have received adequate prior therapy including at a minimum:
         1. Anti-CD20 monoclonal antibody unless investigator determines that tumor is CD20-negative and
         2. An anthracycline containing chemotherapy regimen
         3. For subjects with transformed FL must have received prior chemotherapy for follicular lymphoma and subsequently have chemorefractory disease after transformation to DLBCL
      ii. Do not have the following:
         1. Prior allogeneic HSCT
         2. Active central nervous system malignancy as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
         3. ECOG performance status of 2 or greater
         4. Absolute lymphocyte count less than 100/µL
         5. Creatinine clearance less than 60 mL/min
         6. Hepatic transaminases more than 2.5 times the upper limit of normal
         7. Cardiac ejection fraction less than 50%
         8. Active serious infection
   d. Treatment of adult patients with relapsed or refractory follicular lymphoma (FL)
      i. Subjects must have received at least 2 prior lines of therapy one of which is an anti-CD20 monoclonal antibody combined with an alkylating agent
      ii. Must have measurable disease

iii. Do not have any of the following:
    1. Prior allogeneic HSCT
    2. Active central nervous system malignancy as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
    3. ECOG performance status of 2 or greater
    4. Transformed FL
    5. Histological grade 3b FL
    6. Creatinine clearance less than 60 mL/min
    7. Hepatic transaminases more than 2.5 times the upper limit of normal
    8. Cardiac ejection fraction less than 50%
    9. Active serious infection

e. 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
f. Only to be administered at certified bone marrow/stem cell transplant centers
g. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSNE Part B drugs prior authorization list
h. The prescriber needs to submit documentation of response to Yescarta within 3 months following therapy as a follow-up to the prior approval request
i. 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 Pharmacy and Therapeutics Committee

B. Quantity Limitations, Authorization Period and Renewal Criteria
    a. Quantity Limits: Align with FDA recommended dosing
    b. Authorization Period: 2 months with the allowance of only one dose per lifetime
    c. Renewal Criteria: Not applicable as no further authorization will be provided

C. Preliminary Criteria

****Note: Preliminary criteria only applies if the below listed indications get FDA approval. Coverage will not be granted for any non-approved FDA indications prior to FDA approval****

a. FDA approved age
b. Prescribed by on in consultation with an oncologist
c. Treatment of adult patients with relapsed[a] or refractory[b] large B-cell lymphoma after one line of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, T cell/histiocyte-rich large B-cell lymphoma, DLBCL associated with chronic inflammation, primary cutaneous DLBCL leg type, Epstein-Barr virus positive large B-cell lymphoma, and DLBCL arising from follicular lymphoma (TFL)
    i. Subjects must have received adequate prior therapy with an anti-CD20 monoclonal antibody unless investigator determines that tumor is CD20-negative and an anthracycline containing chemotherapy regimen
    ii. Do not have the following:
        1. Prior allogeneic HSCT
        2. Known or suspected central nervous system involvement as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
        3. ECOG performance status of 2 or greater
        4. Absolute lymphocyte count less than 100/µL
        5. Creatinine clearance less than 60 mL/min

6. Hepatic transaminases more than 2.5 times the upper limit of normal
7. Cardiac ejection fraction less than 50%
8. Active serious infection

e. 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
f. Only to be administered at certified bone marrow/stem cell transplant centers
g. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSNE Part B drugs prior authorization list
h. The prescriber needs to submit documentation of response to Yescarta within 3 months following therapy as a follow-up to the prior approval request
i. 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 Pharmacy and Therapeutics Committee

j. Quantity Limitations, Authorization Period and Renewal Criteria
   i. Quantity Limits: Align with FDA recommended dosing
   ii. Authorization Period: 2 months with the allowance of only one dose per lifetime
   iii. Renewal Criteria: Not applicable as no further authorization will be provided

[a] Relapsed disease defined as complete remission to first-line therapy followed by biopsy-proven relapse ≤ 12 months of first-line therapy

[b] Refractory disease is defined as no complete remission to first-line therapy: progressive disease (PD) as best response to first-line therapy; stable disease (SD) as best response after at least 4 cycles of first-line therapy (eg, 4 cycles of R-CHOP); or partial response (PR) as best response after at least 6 cycles and biopsy-proven residual disease or disease progression ≤ 12 months of therapy.

***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.

- Yescarta 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 not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated

for the treatment of patients with primary central nervous system lymphoma. Yescarta is also indicated for adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

- Efficacy was established in a single-arm, open-label, multicenter trial of 111 adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma. Of 111 patients who underwent leukapheresis, 101 received Yescarta. One patient did not receive the product due to manufacturing failure and 9 others were not treated due to progressive disease or serious adverse reactions. Yescarta was administered as a single intravenous infusion at a target dose of 2×10^6 CAR-positive viable T-cells/kg. The lymphodepleting regimen consisted of cyclophosphamide 500 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously given on the fifth, fourth, and third day before Yescarta. Patients with prior allogeneic HSCT, any history of central nervous system lymphoma, ECOG performance status of 2 or greater, absolute lymphocyte count less than 100/µL, creatinine clearance less than 60 mL/min, hepatic transaminases more than 2.5 times the upper limit of normal, cardiac ejection fraction less than 50%, or active serious infection were excluded. Subjects had previously received an anti-CD20 monoclonal antibody containing-regimen and an anthracycline-containing chemotherapy. Patients with transformed FL had received prior chemotherapy for follicular lymphoma and subsequently have chemorefractory disease after transformation to DLBCL. Primary endpoints were complete remission rate and duration of response. The median time to response was 0.9 months (range: 0.8 to 6.2 months). Of the 52 patients who achieved CR, 14 initially had stable disease (7 patients) or PR (7 patients), with a median time to improvement of 2.1 months (range: 1.6 to 5.3 months).

- Safety and efficacy for use in FL and MZL were established in the ZUMA-5 trial, an ongoing single-arm, open-label, multicenter phase 2 study of 104 adult patients with relapsed/refractory indolent NHL who had received up to 2 prior lines of therapy, including an anti-CD20 monoclonal antibody combined with an alkylating agent. Of the 104 patients, 84 had follicular lymphoma and 20 patients had marginal zone lymphoma and were required to have measurable disease. Patients were excluded if they had prior allogeneic HSCT, any history of central nervous system disease, ECOG performance status of 2 or greater, transformed FL, histological grade 3b FL, inadequate renal, hepatic, or cardiac function, or active serious infection. The primary endpoint is the objective response rate to therapy and key secondary endpoints include duration of response, progression-free survival (PFS), overall survival (OS), and incidence of adverse events. After a median follow-up of 17.5 months, the objective response rate was 92% with 76% of patients reaching a complete response. When broken down by exact indication, 94% (n = 84) of patients with relapsed/refractory FL had an objective response including 80% achieving a complete response. Of patients with relapsed/refractory MZL (n=20), 85% had an objective response with 60% achieving a complete response. At the data cutoff, 62% of all treated patients had ongoing responses. Median duration of response (DOR), progression-free survival (PFS) and overall survival (OS) were not reached.

- Safety and efficacy for use as second-line therapy in relapsed or refractory DLBCL is being established in the ZUMA-7 trial, an ongoing phase 3, randomized, open-label, multicenter study of 359 patients with replased/refractory DLBCL who had received one prior line of therapy that included an anti-CD20 monoclonal antibody combined with an anthracycline agent. Patients with prior allogeneic HSCT, any history of central nervous system lymphoma, ECOG performance status of 2 or greater, absolute lymphocyte count less than 100/µL, creatinine clearance less than 60 mL/min, hepatic transaminases more than 2.5 times the upper limit of normal, cardiac ejection fraction less than 50%, or active serious infection were excluded. Relapsed disease was defined as complete remission to first-line therapy followed by biopsy-proven relapse ≤ 12 months of first-line therapy. Refractory disease was defined as no complete remission to first-line therapy: progressive disease (PD) as best response to first-line therapy; stable disease (SD) as best response after at least 4 cycles of first-line therapy (eg, 4 cycles of R-CHOP); or partial response (PR) as best response after at least 6 cycles and biopsy-proven residual disease or disease progression ≤ 12 months of therapy. The primary endpoint is event-free survival (EFS) defined as time from randomization to disease progression, start of new lymphoma therapy, or death. ZUMA-7 met its primary EFS endpoint demonstrating statistically significant and clinically meaningful improvement in efficacy with Yescarta vs second-line standard of care.

References:

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4. Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10; 124 (2): 188 - 195.
5. Jacobson CA, Chavez JC, Sehgal AR, et al. Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial. Lancet Oncol. 2021 Dec 8; S1470-2045.
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7. Caffrey M. ZUMA-7: axi-cel in second line is the "new standard" in R/R LBCL, locke says. 2021 Dec 12. Available at: https://www.ajmc.com/view/zuma-7-axi-cel-in-second-line-is-the-new-standard-in-r-r-lbcl-locke-says. Accessed on January 6, 2022.

Policy History		
#	Date	Change Description
1.1	Effective Date: 02/10/2022	Updated to include preliminary criteria for use as second-line therapy for DLBCL and remove the CD19 positive requirement
1.0	Effective Date: 08/12/2021	New policy- this policy replaces previously approved criteria that was embedded in Chimeric Antigen Receptor-T Cell Class policy which will be retired

** 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.*