Medicare Advantage Medical Benefit Drug Policy

BlueCross BlueShield Nebraska

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Effective Date: 06/10/2021

Chimeric Antigen Receptor (CAR)-T cell therapy

Abecma® (idecabtagene vicleucel)
Breyanzi® (lisocabtagene maraleucel)
Kymriah™ (tisagenlecleucel)
Tecartus™ (brexucabtagene autoleucel)
Yescarta™ (axicabtagene ciloleucel)

FDA approval: Various
HCPCS: Abecma – J3590, Breyanzi – J3590, C9076, Kymriah – Q2042, Tecartus – Q2053/C9073, Yescarta -Q2041
Benefit: Medical

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 only
      AND
   b. 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
      AND
   c. Only to be administered at certified bone marrow/stem cell transplant centers
      AND
   d. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSNE Part B drugs prior authorization list
   e. Kymriah (tisagenlecleucel)
      i. Prescribed by or in consultation with an oncologist
      ii. Diagnosis of pediatric and young adult with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory[a] or in second or later relapse[b]:
         1. FDA approved age
         2. Primary refractory as defined by not achieving a complete response after 2 cycles of a standard chemotherapy regimen or chemo refractory as defined by not achieving a complete response after 1 cycle of standard chemotherapy for relapsed leukemia

3. Patients with Philadelphia chromosome positive (Ph+) ALL are eligible if they are intolerant to or have failed 2 lines of tyrosine kinase inhibitor therapy (TKI), or if TKI therapy is contraindicated
4. Any bone marrow (BM) relapse after allogenic SCT
5. Do not have any of the following:
    a) Burkitt's lymphoma
    b) Active hepatitis B, C
    c) Any uncontrolled infection
    d) Grade 2 to 4 graft-versus-host disease
    e) Concomitant genetic syndrome with the exception of Down's syndrome
    f) Received allogeneic cellular therapy, such as donor lymphocyte infusion within 6 weeks prior to tisagenlecleucel infusion
6. Documentation of CD 19 tumor expression

iii. Treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma:
1. FDA approved age
2. Received ≥ 2 lines of chemotherapy, including rituximab and anthracycline
OR
3. Relapsed following autologous hematopoietic stem cell transplantation (HSCT)
4. Documentation of CD19 tumor expression
5. Do not have any of the following:
    a) 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)
    b) Prior allogenic HSCT
    c) ECOG performance status ≥ 2
    d) Creatinine clearance < 60 mL/min
    e) Alanine aminotransferase > 5 times normal
    f) Cardiac ejection fraction < 45%
    g) Absolute lymphocyte concentration less than 300/µL

iv. The prescriber needs to submit documentation of response to Kymriah within 3 months following therapy as a follow-up to the prior approval request

v. 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

f. Yescarta (axicabtagene ciloleucel):
i. FDA approved age
ii. Prescribed by or in consultation with an oncologist
iii. 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)
1. Subjects must have received adequate prior therapy including at a minimum:
    a) Anti-CD20 monoclonal antibody unless investigator determines that tumor is CD20-negative and
    b) An anthracycline containing chemotherapy regimen
    c) For subjects with transformed FL must have received prior chemotherapy for follicular lymphoma and subsequently have chemo refractory disease after transformation to DLBCL

2. Documentation of CD19 tumor expression
3. Do not have the following:
    a) Prior allogeneic HSCT
    b) 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)
    c) ECOG performance status of 2 or greater
    d) Absolute lymphocyte count less than 100/µL
    e) Creatinine clearance less than 60 mL/min
    f) Hepatic transaminases more than 2.5 times the upper limit of normal
    g) Cardiac ejection fraction less than 50%
    h) Active serious infection

iv. Treatment of adult patients with relapsed or refractory follicular lymphoma (FL)
1. 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
2. Must have measureable disease
3. Do not have any of the following:
    a) Prior allogeneic HSCT
    b) 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)
    c) ECOG performance status of 2 or greater
    d) Transformed FL
    e) Histological grade 3b FL
    f) Creatinine clearance less than 60 mL/min
    g) Hepatic transaminases more than 2.5 times the upper limit of normal
    h) Cardiac ejection fraction less than 50%
    i) Active serious infection

v. The prescriber needs to submit documentation of response to Yescarta within 3 months following therapy as a follow-up to the prior approval request
vi. 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

g. Tecartus (brexucabtagene autoleucel)
i. FDA approved age
ii. Prescribed by on in consultation with an oncologist
iii. Treatment of adult patients with relapsed or refractory mantle cell lymphoma
iv. Subjects must have received adequate prior therapy including at a minimum:
1. An anthracycline or bendamustine-containing chemotherapy
2. An anti-CD20 monoclonal antibody therapy
3. A Bruton's tyrosine kinase (BTK) inhibitor
v. Must have 1 measurable lesion
vi. Documentation of CD19 tumor expression
vii. Do not have any of the following:
1. ECOG performance status of 2 or greater
2. Absolute neutrophil count < 1,000/µL
3. Platelet count < 75,000/µL
4. Serum alanine aminotransferase/aspartate aminotransferase ≥ 2.5 upper limit of normal
5. Creatinine clearance < 60 mL/min
6. Cardiac ejection fraction < 50%

7. Active infection including hepatitis B, hepatitis C, HIV, or systemic fungal, bacterial, or viral infection
8. Prior allogeneic HSCT
9. 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)

vii. The prescriber needs to submit documentation of response to Tecartus within 3 months following therapy as a follow-up to the prior approval request.
viii. 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.

h. Breyanzi (lisocabtagene maraleucel)
   i. FDA approved age
   ii. Prescribed by on in consultation with an oncologist
   iii. Treatment of patients with relapsed or refractory Non-Hodgkin's lymphoma of the following subtypes:
      1. Diffuse large B-cell lymphoma (DLBCL)
      2. Primary mediastinal B-cell lymphoma (PMBCL)
      3. Follicular lymphoma, grade 3B
   iv. Received ≥ 2 lines of chemotherapy, including rituximab and anthracycline
   OR
   v. Relapsed following autologous hematopoietic stem cell transplantation (HSCT)
   vi. Documentation of CD 19 tumor expression
   vii. Patients must not have the following
      1. ECOG performance status of greater than 2
      2. Creatinine clearance < 30 mL/min
      3. Alanine aminotransferase > 5 times the upper limit of normal
      4. Left ventricular ejection fraction < 40%
      5. Active CNS involvement by primary malignancy (secondary CNS involvement is allowed) as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
      6. History of another primary malignancy that has not been in remission for at least 2 years prior to consideration of CAR-T therapy
      7. Active infection including hepatitis B, hepatitis C, HIV, or systemic fungal, bacterial, or viral infection
      8. Presence of graft-vs-host disease (GVHD)
   viii. The prescriber needs to submit documentation of response to Breyanzi within 3 months following therapy as a follow-up to the prior approval request
   ix. 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

i. Abecma (idecabtagene vicleucel)
   i. FDA approved age
   ii. Prescribed by or in consultation with an oncologist
   iii. Treatment of patients with relapsed or refractory multiple myeloma after at least 4 prior lines of therapy
   iv. Patients must have been treated with all of the following:
      1. An immunomodulatory agent
      2. A proteasome inhibitor
      3. An anti-CD38 antibody

v. Must have active disease defined by at least one of the following:
    1. Serum M-protein greater or equal to 1.0 g/dL
    2. Urine M-protein greater or equal to 200 mg/24 h
    3. Serum free light chain (FLC) assay greater or equal to 10 mg/dL provided the baseline serum FLC ratio is abnormal
vi. Patients must not have the following
    1. ECOG performance status of greater than 2
    2. Known central nervous system involvement with myeloma as determined by appropriate testing. Examples include: MRI and/or CSF analysis (including cytology plus molecular analysis, for example FISH)
    3. Active infection including hepatitis B, hepatitis C, HIV, or systemic fungal, bacterial, or viral infection
    4. Creatinine clearance < 45 ml/min
    5. Alanine aminotransferase > 2.5 times upper limit of normal
    6. Left ventricular ejection fraction < 45%
    7. Absolute neutrophil count < 1000 cells/mm^3
    8. Platelets < 50,000/mm^3
    9. Second malignancies in addition to myeloma if the second malignancy has required therapy in the last 3 years or is not in complete remission
vii. The prescriber needs to submit documentation of response to Abecma within 3 months following therapy as a follow-up to the prior approval request
viii. 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. Initial Authorization Period: 2 months to allow for only one dose per lifetime
    c. Renewal Criteria: N/A
    d. Renewal Authorization Period: No renewal allowed

[a] Refractory (resistant) disease is defined as those patients who fail to obtain complete response with induction therapy, ie. failure to eradicate all detectable leukemia cells (<5% blasts) from the bone marrow and blood with subsequent restoration of normal hematopoiesis (>25% marrow cellularity and normal peripheral blood counts)

[b] Relapsed disease describes the reappearance of leukemia cells in the bone marrow or peripheral blood after the attainment of a complete remission with chemotherapy and/or allogeneic stem cell transplant Legend

***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.

Therapeutic considerations:

A. **FDA Approved Indication/Diagnosis:**

**Please refer to most recent prescribing information.*

B. **Background Information**

a. 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.

b. 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.

c. 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.

d. Kymriah:

i. Kymriah is indicated for patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. It is also approved for use in adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including DLBCL not otherwise specified, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated for treatment of patients with primary central nervous system lymphoma.

ii. Safety and efficacy was established in two studies. The first was the ELIANA trial, an open-label, multicenter single-arm study of 107 pediatric and young adult patients with relapsed/refractory B-cell precursor ALL. All patients were screened, 88 were enrolled in the study, 68 were treated with CAR-T, and 63 were evaluable for efficacy. Nine percent of the enrolled subjects did not receive the product due to manufacturing failure. Treatment consisted of lymphodepleting chemotherapy (fludarabine 30 mg/m2 daily for 4 days and cyclophosphamide 500 mg/m2 daily for 2 days) followed by a single dose of Kymriah. Tumors must have had CD19 expressing tumor cells. Patients were included if they were primary refractory defined as not achieving a complete response after 2 cycles of a standard chemotherapy regimen or chemorefractory as defined by not achieving a complete response after 1 cycle of standard chemotherapy for relapsed leukemia; has Philadelphia chromosome positive (Ph+) ALL and were intolerant to or failed 2 lines of tyrosine kinase inhibitor therapy (TKI) or if TKI therapy was contraindicated; they were ineligible for allogeneic stem cell transplant (SCT); or had any bone marrow (BM) relapse after allogenic SCT. Patients were excluded if they had Burkitt's lymphoma, active hepatitis B or C, any uncontrolled infection, grade 2 to 4 graft-versus-host disease, concomitant genetic syndrome with the exception of Down's syndrome, or if they have received allogeneic cellular therapy, such as donor lymphocyte infusion within 6 weeks prior to Kymriah infusion. Efficacy was based on complete remission (CR) within 3 months after infusion, the duration of CR, and proportion of patients with CR and minimal residual disease (MRD) < 0.01% by flow cytometry (MRD-negative). Among the 63 infused patients, 52 (83%) achieved CR/CRi, all of which were MRD-negative. With a median follow-up of 4.8 months from response, the median duration of CR/CRi was not reached (range: 1.2 to 14.1+ months). Median time to onset of CR/CRi was 29 days with onset of CR/CRi between 26 and 31 days for 50/52 (96%) responders. The stem cell transplantation rate among those who achieved CR/CRi was 12% (6/52).

iii. Efficacy was also established in the JULIET trial, an open-label, multicenter, single-arm trial of 160 adult patients with relapsed or refractory DLBCL, who received ≥ 2 lines of chemotherapy, including rituximab and anthracycline, or relapsed following autologous hematopoietic stem cell transplantation (HSCT). Of the160 patients enrolled, 106 patients received Kymriah. Eleven patients enrolled did not receive Kymriah due to manufacturing failure and 38 other patients did not receive Kymriah due to death (n = 16), physician decision (n = 16), or adverse events (n = 3). Patients with active central nervous system malignancy, prior allogenic HSCT, an ECOG performance status ≥ 2, a creatinine clearance < 60, alanine aminotransferase > 5 times normal, cardiac ejection fraction < 45%, or absolute lymphocyte concentration less than 300/µL were excluded from the study. The primary endpoints were complete response (CR) rate and duration of response (DOR). The median time to first response was 0.9 months (range: 0.7 to 3.3 months). The median duration of response was not reached. Response durations were longer in patients who achieved CR as compared to patients with a best response of partial response (PR). Of the 22 patients who experienced a CR, 9 achieved this status by 1 month, 12 more by month 3, and the last by month 6 after Kymriah infusion.

e. Yescarta

i. 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.

ii. 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).

iii. Safety and efficacy for use in FL and MZL are being established in the ZUMA-5 trial, a 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 or MZL, 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.

f. Tecartus

i. Tecartus is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

ii. Safety and efficacy were established in the ZUMA-2 trial, a single-arm, open-label, multicenter phase II study of 74 adult patients with relapsed or refractory mantle cell lymphoma. Patients had received up to 5 prior lines of therapy, including an anti-CD20 antibody, either an anthracycline- or bendamustine-containing chemotherapy regimen, and a Bruton's tyrosine kinase (BTK) inhibitor. Three patients experienced manufacturing failure, one died of progressive disease, and one withdrew from the study prior to lymphodepleting chemotherapy. One patient received lymphodepleting chemotherapy but did not receive Tecartus due to ongoing active atrial fibrillation. Tecartus 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 Tecartus. Patients with prior allogeneic HSCT, any active central nervous system malignancy, ECOG performance status of 2 or greater, absolute neutrophil count less than 1,000/µL, platelet count < 75,000/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. The primary endpoint was objective response rate to therapy which was 87%, including 37 patients who had complete response (62%) and 15 who had a partial response (25%). The median time to response was 28 days with median duration of response not yet being reached.

g. Breyanzi

i. 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.

ii. Safety and efficacy 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 patient's who received previous CD19-targeted therapy, CD19-positive lymphoma

confirmed on a biopsy had to be confirmed since completing the prior CD19-targeted therapy. Patient's 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.

h. Abecma

i. Abecma is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

ii. Safety and efficacy were established in the KarMMa trial, an open-label, single-arm, multicenter study of 127 patients with relapsed or refractory multiple myeloma who had received at least three prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. The study excluded patients with an ECOG score of 2 or greater, a creatinine clearance of less than or equal to 45 mL/minute, alanine aminotransferase greater than 2.5 times upper limit of normal, and left ventricular ejection fraction less than 45%. Patients were also excluded if absolute neutrophil count less than 1000 cells/mm^3 and platelet count less than 50,000/mm^3. Patients were required to have measurable disease. The primary endpoints included overall response rate (ORR), complete response (CR), and duration of response (DOR). The ORR was 72% (95% CI: 62 - 81) with 28% of patients achieving a stringent complete response (sCR; 95% CI: 19 - 38). Responses were rapid and durable with a median time to response of 30 days (range: 15 to 88 days) and median duration of response of 11 months (95% CI: 10.3 – 11.4) for all responders and 19 months (95% CI: 11.4 – NE) for those who achieved a sCR. Of the 28 patients who achieved sCR, an estimated 65% (95% CI: 42% - 81%) had remission lasting at least 12 months.

i. 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).

C. **Efficacy**

**Please refer to most recent prescribing information.*

D. **Medication Safety Considerations**

**Please refer to most recent prescribing information.*

E. **Dosing and administration**

**Please refer to most recent prescribing information.*

F. **How supplied**

**Please refer to most recent prescribing information.*

References:

1. Kymriah [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018
2. Yescarta [prescribing information]. Santa Monica, CA: Kite Pharma, Inc.; March 2021.
3. Tecartus [prescribing information]. Santa Monica, CA: Kite Pharma, Inc,; July 2020.
4. Breyanzi [prescribing information]. Bothell, WA: Bristol Myers Squibb; February 2021.
5. Abecma [prescribing information]. Summit, NJ: Celgene Corporation, a Bristol-Myers Squibb Company; March 2021.
6. Clinicaltrials.gov. A phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019 in pediatric patients with relapsed and refractory b-cell acute lymphoblastic leukemia. Available at: https://clinicaltrials.gov/ct2/show/study/NCT02435849. Accessed on August 3, 2017.
7. LaRussa A. Chimeric antigen receptor (CAR) t-cell therapy. 10 Sept. 2015. Available at: www.lls.org/treatment/types-of-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy. Access on August 3, 2017.
8. National Comprehensive Cancer Network. Pediatric acute lymphoblastic leukemia (Version 2.2020). 2019 Nov 25. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed on June 10, 2020.
9. National Comprehensive Cancer Network. Adult acute lymphoblastic leukemia (Version 1.2020). 2020 Jan 15. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed on June 10, 2020.
10. National Comprehensive Cancer Network. B-cell lymphomas (Version 1.2021). 2021 Jan 20. Available at: https:// www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on February 8, 2021.
11. Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood. 2014 Jul 10; 124 (2): 188 - 195.
12. Clinicaltrials.gov. A phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019 in adult patients with relapsed or refractory diffuse large b-cell lymphoma (DLBCL). Available at: https://clinicaltrials.gov/ct2/show/NCT02445248. Accessed on August 3, 2017.
13. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle cell lymphoma. NEJM. 2020 Apr 2; 382 (14): 1331 – 42.
14. Clinicaltrials.gov. A phase 2 multicenter study of axicabtagene ciloleucel in subjects with relapsed/refractory indolent non-hodgkin lymphoma (NCT03105336). Available at: https://clinicaltrials.gov/ct2/show/NCT03105336. Accessed on December 10, 2020.
15. 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.
16. 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.

17. Jacobson C, Chavez JC, Sehgal AR, et al. Primary analysis of zuma-5: a phase 2 study of axicabtagene ciloleucel (Axi-Cel) in patients with relapsed/refractory (R/R) indolent non-hodgkin lymphoma (iNHL). Blood. 2020 Nov 5; 136 (Suppl 1): 40 – 1.
18. 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.
19. National Comprehensive Cancer Network. Multiple myeloma (Version 5.2021). 2021 March 15. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed on March 29, 2021.
20. Munshi NC, Anderson Jr LD, Shah N, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. NEJM. 2021 Feb 25; 384 (8): 705 - 16.

Policy History		
#	Date	Change Description
1.1	Effective Date: 06/10/2021	Updated to add Abecma
1.0	Effective Date: 06/01/2021	Medical policy established

** 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.*