Corporate Medical Policy: CAR-T Therapy **POLICY EFFECTIVE JUNE 16, 2021**

Restricted Product(s):

- axicabtagene ciloleucel (Yescarta®) intravenous infusion for administration by a healthcare professional
- brexucabtagene autoleucel (Tecartus®) intravenous infusion for administration by a healthcare professional
- idecabtagene vicleucel (Abecma®) intravenous infusion for administration by a healthcare professional
- lisocabtagene maraleucel (Breyanzi®) intravenous infusion for administration by a healthcare professional
- tisagenlecleucel (Kymriah®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- Axicabtagene ciloleucel (Yescarta®)
  - For treatment of adults 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, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma
    - Limitations of use: Not for treatment of primary central nervous system lymphoma
  - For treatment of adults with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy
- Brexucabtagene autoleucel (Tecartus®)
  - For treatment of adults with relapsed or refractory mantle cell lymphoma (MCL)
- Idecabtagene vicleucel (Abecma®)
  - For treatment of adults 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
- Lisocabtagene maraleucel (Breyanzi®)
  - For treatment of adults 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
    - Limitations of use: Not for treatment of primary central nervous system lymphoma
- Tisagenlecleucel (Kymriah®)
  - For treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
  - For treatment of adults 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, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma

- Limitations of use: Not for treatment of primary central nervous system lymphoma

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The request is for **tisagenlecleucel (Kymriah)**; **AND**
    a. The patient has a diagnosis of **relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)**; **AND**
        i. The patient is 25 years of age or younger; **AND**
        ii. The patient has a confirmed CD19 tumor expression **[medical record documentation required]**; **AND**
        iii. The patient has not previously received genetically modified T cell therapy or tisagenlecleucel **(**Kymriah) **[medical record documentation required]**; **AND**
        iv. For patients with Philadelphia Chromosome positive (Ph+) ALL, one of the following:
            1. The patient has tried and had an inadequate response to at least two tyrosine kinase inhibitors (TKI) **[medical record documentation required]**; **OR**
            2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL TKIs used in the treatment of ALL **[medical record documentation required]**; **AND**
        v. The patient has received or will receive a lymphodepleting chemotherapy regimen of fludarabine 30 mg/m^2 intravenously daily for 4 days and cyclophosphamide 500 mg/m^2 intravenously daily for 2 days starting with the first dose of fludarabine, within two weeks prior to infusion of tisagenlecleucel **(**Kymriah) **[medical record documentation required]**; **AND**
        vi. The patient will not be treated with more than 2.5 x 10^8 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
        vii. If the patient weighs ≤ 50 kg, they will receive weight-based dosing of 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg of body weight **[documentation of planned dosage required]**; **AND**
        viii. One of the following:
            1. The patient has been treated with two cycles of standard chemotherapy without a complete response **[medical record documentation required]**; **OR**
            2. The patient achieved a complete response and experienced multiple relapses following standard chemotherapy (at least 2 cycles) **[medical record documentation required]**; **AND**
        ix. The patient does not have active central nervous system (CNS) 3 acute lymphoblastic leukemia **[medical record documentation required]**; **OR**
    b. The patient has a diagnosis of **relapsed or refractory B-cell lymphoma** including any of the following **[medical record documentation required]**:

1. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
2. High grade B-cell lymphoma
3. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma; **AND**

ii. The patient is 18 years of age or older; **AND**
iii. The patient has not previously received genetically modified T cell therapy or tisagenlecleucel **(**Kymriah) **[medical record documentation required]**; **AND**
iv. The patient has experienced disease progression following a trial of two or more lines of systemic therapy **[medical record documentation required]**; **AND**
v. Previous therapy included an anthracycline chemotherapy agent and an anti-CD20 antibody **[medical record documentation required]**; **AND**
vi. One of the following:
    1. The patient has received or will receive a lymphodepleting chemotherapy regimen of fludarabine 25 mg/m^2 intravenously daily for 3 days and cyclophosphamide 250 mg/m^2 intravenously daily for 3 days starting with the first dose of fludarabine, or alternate therapy with bendamustine 90 mg/m^2 intravenously daily for 2 days for patients unable to receive cyclophosphamide, within two weeks prior to infusion of tisagenlecleucel **(**Kymriah) **[medical record documentation required]**; **OR**
    2. The patient is unable to receive lymphodepleting chemotherapy if WBC count is ≤ 1x10^9 /L within one week prior to tisagenlecleucel **(**Kymriah) infusion **[medical record documentation required]**; **AND**
vii. The patient will be treated within a dosage range of 0.6 to 6.0 x 10^8 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
viii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **AND**
ix. The patient does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV), or any autoimmune disease requiring immune suppression; **OR**

2. The request is for **axicabtagene ciloleucel (Yescarta)**; **AND**
    a. The patient has a diagnosis of **relapsed or refractory B-cell lymphoma** including any of the following **[medical record documentation required]**:
        1. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
        2. Primary mediastinal large B-cell lymphoma
        3. High grade B-cell lymphoma
        4. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma; **AND**

    ii. The patient is 18 years of age or older; **AND**

iii. The patient has not previously received genetically modified T cell therapy or axicabtagene ciloleucel (Yescarta) **[medical record documentation required]**; **AND**
iv. The patient has experienced disease progression following a trial of two or more lines of systemic therapy **[medical record documentation required]**; **AND**
v. Previous therapy included an anthracycline chemotherapy agent and an anti-CD20 antibody **[medical record documentation required]**; **AND**
vi. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously on the fifth, fourth, and third days before infusion of axicabtagene ciloleucel (Yescarta) **[medical record documentation required]**; **AND**
vii. The patient will not be treated with more than 2 x 10^8 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
viii. The patient will receive a target dose of 2 x 10^6 CAR-positive viable T cells per kg body weight **[documentation of planned dosage required]**; **AND**
ix. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **AND**
x. The patient does not have does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV), or any autoimmune disease requiring immune suppression; **OR**

b. The patient has a diagnosis of **relapsed or refractory follicular lymphoma [medical record documentation required]**; **AND**
i. The patient is 18 years of age or older; **AND**
ii. The patient has not previously received genetically modified T cell therapy or axicabtagene ciloleucel (Yescarta) **[medical record documentation required]**; **AND**
iii. The patient has experienced disease progression following a trial of two or more lines of systemic therapy **[medical record documentation required]**; **AND**
iv. Previous therapy included a combination of an anti-CD20 antibody and an alkylating agent **[medical record documentation required]**; **AND**
v. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously on the fifth, fourth, and third days before infusion of axicabtagene ciloleucel (Yescarta) **[medical record documentation required]**; **AND**
vi. The patient will receive a target dose of 2 x 10^6 CAR-positive viable T cells per kg body weight **[documentation of planned dosage required]**; **AND**
vii. The patient does not have does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV), or any autoimmune disease requiring immune suppression; **OR**

3. The request is for **brexucabtagene autoleucel (Tecartus)**; **AND**
    a. The patient has a diagnosis of **relapsed or refractory mantle cell lymphoma (MCL) [medical record documentation required]**; **AND**
    b. The patient is 18 years of age and older; **AND**
    c. The patient has been treated with ALL of the following **[medical record documentation required]**:
        i. An anthracycline or bendamustine-containing chemotherapy; **AND**
        ii. Anti-CD20 monoclonal antibody therapy (e.g., rituximab); **AND**
        iii. A Bruton tyrosine kinase (BTK) inhibitor indicated for mantle cell lymphoma (e.g., acalabrutinib, ibrutinib); **AND**
    d. The patient has disease progression after their last regimen or refractory disease to the most recent therapy **[medical record documentation required]**; **AND**
    e. The patient has not had a prior allogeneic hematopoietic stem cell transplant (HSCT) **[medical record documentation required]**; **AND**
    f. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously on each of the fifth, fourth, and third days before infusion of brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
    g. The patient will not be treated with more than 2 x 10^8 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
    h. The patient has not previously received genetically modified T cell therapy or brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
    i. The patient does not have detectable malignant cells in the cerebrospinal fluid or brain metastases **[medical record documentation required]**; **AND**
    j. The patient does not have any history of central nervous system (CNS) lymphoma **[medical record documentation required]**; **AND**
    k. The patient does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV); **OR**

4. The requested agent is **lisocabtagene maraleucel (Breyanzi)**; **AND**
    a. The patient has a diagnosis of **relapsed or refractory B-cell lymphoma** including any of the following **[medical record documentation required]**:
        i. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma)
        ii. Primary mediastinal large B-cell lymphoma
        iii. High grade B-cell lymphoma
        iv. Follicular lymphoma grade 3B; **AND**
    b. The patient is 18 years of age or older; **AND**

c. The patient has not previously received genetically modified T cell therapy or lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
d. The patient has experienced disease progression following a trial of two or more lines of systemic therapy **[medical record documentation required]**; **AND**
e. Previous therapy included an anthracycline chemotherapy agent and an anti-CD20 antibody **[medical record documentation required]**; **AND**
f. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 300 mg/m^2/day intravenously and fludarabine 30 mg/m^2/day intravenously daily for 3 days before infusion of lisocabtagene maraleucel **(**Breyanzi) **[medical record documentation required]**; **AND**
g. The patient will NOT be treated with more than 110 x 10^6 CAR-positive viable T cells (consisting of CD8 and CD4 components) **[documentation of planned dosage required]**; **AND**
h. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **AND**
i. The patient does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV); **OR**

5. The requested agent is **idecabtagene vicleucel (Abecma)**; **AND**
   a. The patient has a diagnosis of **relapsed or refractory multiple myeloma [medical record documentation required]**; **AND**
   b. The patient is 18 years of age or older; **AND**
   c. The patient has not previously received genetically modified T cell therapy or idecabtagene vicleucel (Abecma) **[medical record documentation required]**; **AND**
   d. The patient has experienced disease progression following a trial of four or more lines of systemic therapy **[medical record documentation required]**; **AND**
   e. Previous therapy included an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody **[medical record documentation required]**; **AND**
   f. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 300 mg/m^2 intravenously and fludarabine 30 mg/m^2 intravenously daily for 3 days before infusion of idecabtagene vicleucel (Abecma) **[medical record documentation required]**; **AND**
   g. The patient will NOT be treated with more than 460 x 10^6 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
   h. The patient has NOT had a prior allogeneic hematopoietic stem cell transplant (HSCT) **[medical record documentation required]**; **AND**
   i. The patient does not have active infection including Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV).

Duration of Approval: One treatment course per lifetime

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
axicabtagene ciloleucel (Yescarta®) intravenous (IV) infusion	Relapsed or refractory large B-cell lymphoma Relapsed or refractory follicular lymphoma (FL)	Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. Target dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells via IV infusion	Q2041	**1 unit**
brexucabtagene autoleucel (Tecartus®) intravenous (IV) infusion	Relapsed or refractory mantle cell lymphoma (MCL)	Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. Dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells via IV infusion	Q2053	**1 unit**
idecabtagene vicleucel (Abecma®) intravenous (IV) infusion	Relapsed or refractory multiple myeloma	Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. Dose is 300 to 460×10^6 CAR-positive viable T cells via IV infusion	C9399** J3490** J3590** J9999**	**1 unit**

lisocabtagene maraleucel (Breyanzi®) intravenous (IV) infusion	Relapsed or refractory large B-cell lymphoma	Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. Dose is 50 to 110 × 10^6 CAR-positive viable T cells (consisting of CD8 and CD4 components) via IV infusion	C9399** J3490** J3590** J9999**	**1 unit**
tisagenlecleucel (Kymriah®) intravenous (IV) infusion	Relapsed/Refractory B-cell precursor acute lymphoblastic leukemia (ALL) Patients up to 25 years of age with relapsed or refractory large B-cell lymphoma	**Pediatric and Young Adult B-cell ALL:** Patients ≤50 kg administer 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg body weight via IV infusion Patient >50 kg, administer 0.1 to 2.5 x 10^8 total CAR-positive viable T cells (non-weight based) via IV infusion **Relapsed or Refractory Diffuse Large B-cell Lymphoma:** 0.6 to 6.0 x 10^8 CAR-positive viable T cells via IV infusion	Q2042	**1 unit**

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

Other related CPT codes for CAR-T Therapy: 0537T, 0538T, 0539T, 0540T

Please note the following HCPCS code descriptions:

- Q2041 – Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

- Q2042 – Tisagenlecleucel, up to 600 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
- Q2053 – Brexucabtagene autoleucel, up to 200 million autologous anti-CD19 CAR positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information:

June 2021: Criteria change: Removed specific weight dosing within Yescarta criteria based on updated FDA label; added requirement of documentation of planned dose; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**. *Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.

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- You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, Civil Rights Coordinator - Privacy, Ethics & Corporate Policy Office is available to help you.

- You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at *https://ocrportal.hhs.gov/ocr/portal/lobby.jsf,* or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 **1-800-368-1019, 800-537-7697** (TDD). Complaint forms are available at *http://www.hhs.gov/ocr/office/file/index.html.*

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1-888-206-4697 (TTY: 1- 800-442-7028)번으로 전화해 주십시오.

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ملحوظة: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم
1-888-206-4697. المبرقة الكاتبة: 1-800-442-7028.

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau
1-888-206-4697 (TTY: 1-800-442-7028).

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-888-206-4697 (телетайп: 1-800-442-7028).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-888-206-4697 (TTY: 1-800-442-7028).

સુચના: જો તમે ગુજરાતી બોલતા હો, તો નિ:સુલ્ક ભાષા સહાય સેવાઓ તમારા માટે ઉપલબ્ધ છે. ફોન કરો
1-888-206-4697 (TTY: 1-800-442-7028).

ចំណាំ៖ ប្រសិនបើលោកអ្នកនិយាយជាភាសាខ្មែរ សេវាកម្មជំនួយផ្នែកភាសាមានផ្តល់ជូនសម្រាប់លោកអ្នកដោយមិនគិតថ្លៃ។ សូមទំនាក់ទំនងតាមរយៈលេខ៖ 1-888-206-4697 (TTY: 1-800-442-7028)។

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-888-206-4697 (TTY: 1-800-442-7028).

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ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-888-206-4697 (TTY: 1-800-442-7028).

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