**Corporate Medical Policy:** CAR-T Therapy

**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
- ciltacabtagene autoleucel (Carvykti®) 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
- obecabtagene autoleucel (Aucatzyl®) 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 large B-cell lymphoma:
    - That is relapsed or refractory 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; or
    - That is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
    - 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)
  - For treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)
- Ciltacabtagene autoleucel (Carvykti®)
  - For treatment of adults with relapsed or refractory multiple myeloma who have received at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide
- Idecabtagene vicleucel (Abecma®)
  - For treatment of adults with relapsed or refractory multiple myeloma after two 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 large B-cell lymphoma, 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, who have:
        - Relapsed or refractory disease after two or more lines of systemic therapy; or
        - Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy; or
        - Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
        - Limitations of use: Not for treatment of primary central nervous system lymphoma
    - For treatment of adults with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least two prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor
    - For treatment of adults with relapsed or refractory follicular lymphoma (FL) who have received two or more prior lines of systemic therapy
    - For treatment of adults with relapsed or refractory mantle cell lymphoma (MCL) who have received at least two prior lines of systemic therapy, including a Bruton tyrosine kinase (BTK) inhibitor
- Obecabtagene autoleucel (Aucatzyl®)
    - For treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)
- 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
    - For treatment of adults with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy

**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) [medical record documentation required]**; **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**
    i. The patient is 18 years of age or older; **AND**

ii. The patient has not previously received genetically modified T cell therapy or tisagenlecleucel (Kymriah) **[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 an anthracycline chemotherapy agent and an anti-CD20 antibody **[medical record documentation required]**; **AND**
v. 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**
vi. 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**
vii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

c. 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 tisagenlecleucel (Kymriah) **[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. 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 one week 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**

vi. 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]**; **OR**

2. The request is for **axicabtagene ciloleucel (Yescarta)**; **AND**
   a. The patient has a diagnosis of **relapsed or refractory B-cell 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. ONE of the following:
         1. The patient has experienced disease progression following a trial of two or more lines of systemic therapy, including any of the following types **[medical record documentation required]**:
            a. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
            b. Primary mediastinal large B-cell lymphoma
            c. High grade B-cell lymphoma
            d. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma; **OR**
         2. The patient has experienced disease progression following first-line chemoimmunotherapy **[medical record documentation required]**; **AND**
      iv. Previous therapy included an anthracycline chemotherapy agent and an anti-CD20 antibody **[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 not be treated with more than 2 x $10^8$ CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
      vii. 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**
      viii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **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]**; **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**
      i. The patient is 18 years of age or older; **AND**
      ii. The patient has been treated with ALL of the following **[medical record documentation required]**:
         1. An anthracycline or bendamustine-containing chemotherapy; **AND**
         2. Anti-CD20 monoclonal antibody therapy (e.g., rituximab); **AND**
         3. A Bruton tyrosine kinase (BTK) inhibitor indicated for mantle cell lymphoma (e.g., acalabrutinib, ibrutinib); **AND**
      iii. The patient has disease progression after their last regimen or refractory disease to the most recent therapy **[medical record documentation required]**; **AND**
      iv. The patient has not had a prior allogeneic hematopoietic stem cell transplant (HSCT) **[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 each of the fifth, fourth, and third days before infusion of brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
      vi. The patient will not be treated with more than 2 x $10^8$ CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
      vii. The patient has not previously received genetically modified T cell therapy or brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
      viii. The patient does not have detectable malignant cells in the cerebrospinal fluid or brain metastases **[medical record documentation required]**; **AND**

ix. The patient does not have any history of central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

b. The patient has a diagnosis of **relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) [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 brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
   iii. 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**
   iv. The patient has received or will receive a lymphodepleting chemotherapy regimen of fludarabine 25 mg/$m^2$ intravenously on the fourth, third, and second day and cyclophosphamide 900 mg/$m^2$ intravenously on the second day prior to infusion of brexucabtagene autoleucel (Tecartus) **[medical record documentation required]**; **AND**
   v. The patient will not be treated with more than 1 x $10^8$ CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
   vi. One of the following:
      1. The patient has primary refractory disease that 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 first relapse following a remission lasting ≤ 12 months **[medical record documentation required]**; **OR**
      3. The patient has relapsed or refractory disease after two or more lines of systemic therapy **[medical record documentation required]**; **OR**
      4. The patient has relapsed or refractory disease after at least 100 days post-allogeneic stem cell transplantation (HSCT) **[medical record documentation required]**; **AND**
   vii. The patient does not have any history of CNS disorders, including CNS-2 disease with neurologic changes and CNS-3 disease **[medical record documentation required]**; **OR**

4. The request is for **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]**:

1. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma)
2. Primary mediastinal large B-cell lymphoma
3. High grade B-cell lymphoma
4. Follicular lymphoma grade 3B; **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 lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
iii. ONE of the following:
    1. The patient has experienced disease progression following a trial of two or more lines of systemic therapy **[medical record documentation required]**; **OR**
    2. The patient has refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy **[medical record documentation required]**; **OR**
    3. The patient has refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy, and the patient is not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age **[medical record documentation required]**; **AND**
iv. Previous therapy included an anthracycline chemotherapy agent and an anti-CD20 antibody **[medical record documentation required]**; **AND**
v. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 300 mg/$m^2$ intravenously daily and fludarabine 30 mg/$m^2$ intravenously daily for 3 days before infusion of lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
vi. 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**
vii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

b. The patient has a diagnosis of **relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) [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 lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
    iii. The patient has experienced disease progression following a trial of two or more prior lines of systemic therapy **[medical record documentation required]**; **AND**
    iv. Previous therapy included a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor **[medical record documentation required]**; **AND**

v. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 300 mg/m$^2$ intravenously daily and fludarabine 30 mg/m$^2$ intravenously daily for 3 days before infusion of lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
vi. The patient will be treated within a dosage range of 90 to 110 x 10$^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) **[documentation of planned dosage required]**; **AND**
vii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

c. 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 lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
   iii. The patient has experienced disease progression following a trial of two or more prior 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 300 mg/m$^2$ intravenously daily and fludarabine 30 mg/m$^2$ intravenously daily for 3 days before infusion of lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
   vi. The patient will be treated within a dosage range of 90 to 110 x 10$^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) **[documentation of planned dosage required]**; **AND**
   vii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

d. The patient has a diagnosis of **relapsed or refractory mantle cell lymphoma (MCL) [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 lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**
   iii. The patient has experienced disease progression following a trial of two or more prior lines of systemic therapy **[medical record documentation required]**; **AND**
   iv. Previous therapy included ALL of the following **[medical record documentation required]**:
      1. An alkylating agent (e.g., bendamustine); **AND**
      2. Anti-CD20 monoclonal antibody therapy (e.g., rituximab); **AND**

3. A Bruton tyrosine kinase (BTK) inhibitor indicated for mantle cell lymphoma (e.g., acalabrutinib, ibrutinib, zanubrutinib, pirtobrutinib); **AND**

v. The patient has received or will receive a lymphodepleting chemotherapy regimen of cyclophosphamide 300 mg/m$^2$ intravenously daily and fludarabine 30 mg/m$^2$ intravenously daily for 3 days before infusion of lisocabtagene maraleucel (Breyanzi) **[medical record documentation required]**; **AND**

vi. The patient will be treated within a dosage range of 90 to 110 x 10$^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) **[documentation of planned dosage required]**; **AND**

vii. The patient does not have primary central nervous system (CNS) lymphoma **[medical record documentation required]**; **OR**

5. The request is for **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 two 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 510 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]**; **OR**

6. The request is for **ciltacabtagene autoleucel (Carvykti)**; **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 ciltacabtagene autoleucel (Carvykti) **[medical record documentation required]**; **AND**
   d. The patient has experienced disease progression following a trial of at least one prior line of systemic therapy **[medical record documentation required]**; **AND**

e. Previous therapy included an immunomodulatory agent and a proteasome inhibitor **[medical record documentation required]**; **AND**
f. The patient is refractory to lenalidomide treatment **[medical record documentation required]**; **AND**
g. 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 ciltacabtagene autoleucel (Carvykti) **[medical record documentation required]**; **AND**
h. The patient will NOT be treated with more than 1 x $10^8$ CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
i. The patient has NOT had a prior allogeneic hematopoietic stem cell transplant (HSCT) **[medical record documentation required]**; **OR**

7. The request is for **obecabtagene autoleucel (Aucatzyl)**; **AND**
   a. The patient has a diagnosis of **relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) [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 obecabtagene autoleucel (Aucatzyl) **[medical record documentation required]**; **AND**
   d. For patients with Philadelphia Chromosome positive (Ph+) ALL, one of the following:
      i. The patient has tried and had an inadequate response to at least two tyrosine kinase inhibitors (TKI) **[medical record documentation required]**; **OR**
      ii. The patient has tried and had an inadequate response to at least one second-generation TKI **[medical record documentation required]**; **OR**
      iii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL TKIs used in the treatment of ALL **[medical record documentation required]**; **AND**
   e. ONE of the following:
      i. The patient has primary refractory disease that has been treated with two cycles of standard chemotherapy without a complete response **[medical record documentation required]**; **OR**
      ii. The patient achieved a complete response and experienced first relapse following a remission lasting ≤ 12 months **[medical record documentation required]**; **OR**
      iii. The patient has relapsed or refractory disease after two or more lines of systemic therapy **[medical record documentation required]**; **OR**
      iv. The patient has relapsed or refractory disease after at least 3 months post-allogeneic stem cell transplantation (HSCT) **[medical record documentation required]**; **AND**

f. 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) before infusion of obecabtagene autoleucel (Aucatzyl) **[medical record documentation required]**; **AND**
g. The patient has NOT received other anti-CD19 therapy (e.g., blinatumomab) OR patient previously received other anti-CD19 therapy and re-biopsy indicates CD-19 positive disease **[medical record documentation required]**; **AND**
h. The patient will NOT be treated with more than 410 x $10^6$ CD19 CAR-positive viable T cells **[documentation of planned dosage required]**; **AND**
i. The patient does not have any history of CNS disorders, including CNS-2 disease with neurologic changes and CNS-3 disease **[medical record documentation required]**.

**Duration of Approval:** 180 days (one treatment course per lifetime)

| FDA Label Reference | | | | |
|---|---|---|---|---|
| **Medication** | **Indication** | **Dosing** | **HCPCS** | **Maximum Units*** |
| axicabtagene ciloleucel (Yescarta®)<br><br>intravenous (IV) infusion | Relapsed or refractory large B-cell lymphoma<br><br>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®)<br><br>intravenous (IV) infusion | Relapsed or refractory mantle cell lymphoma (MCL)<br><br>Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) | Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells.<br><br>**MCL:**<br>Dose is 2 × $10^6$ CAR-positive viable T cells per kg body weight, with a | Q2053 | **1 unit** |

| FDA Label Reference | | | | |
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| **Medication** | **Indication** | **Dosing** | **HCPCS** | **Maximum Units*** |
| | | maximum of 2 × $10^8$ CAR-positive viable T cells, via IV infusion<br><br>**B-cell ALL:**<br>Dose is 1 x $10^6$ CAR-positive viable T cells per kg body weight, with a maximum of 1 x $10^8$ CAR-positive viable T cells, via IV Infusion | | |
| ciltacabtagene autoleucel (Carvykti®)<br><br>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 0.5 to 1.0 × $10^6$ CAR-positive viable T cells per kg of body weight, with a maximum dose of 1 × $10^8$ CAR-positive viable T cells, via IV infusion. | Q2056 | **1 unit** |
| idecabtagene vicleucel (Abecma®)<br><br>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 510 × $10^6$ CAR-positive viable T cells via IV infusion. | Q2055 | **1 unit** |
| lisocabtagene maraleucel (Breyanzi®)<br><br>intravenous (IV) infusion | Relapsed or refractory large B-cell lymphoma (LBCL) | Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. | Q2054 | **1 unit** |

| FDA Label Reference | | | | |
|---|---|---|---|---|
| **Medication** | **Indication** | **Dosing** | **HCPCS** | **Maximum Units*** |
| | Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) | For LBCL after one line of therapy: Dose is 90 to 110 × $10^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) via IV infusion<br><br>For LBCL after two or more lines of therapy: Dose is 50 to 110 × $10^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) via IV infusion<br><br>For CLL and SLL: Dose is 90 to 110 × $10^6$ CAR-positive viable T cells (consisting of CD8 and CD4 components) via IV infusion | | |
| obecabtagene autoleucel (Aucatzyl®)<br><br>intravenous (IV) infusion | Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) | Total dose is 410 × $10^6$ CD19 CAR-positive viable T cells via IV infusion, as a split dose administered on day 1 and day 10 (± 2 days) determined by patient bone marrow blast assessment | C9301<br>J3490**<br>J3590**<br>J9999** | **1 unit** |

| FDA Label Reference | | | | |
|---|---|---|---|---|
| **Medication** | **Indication** | **Dosing** | **HCPCS** | **Maximum Units*** |
| tisagenlecleucel (Kymriah®)<br>intravenous (IV) infusion | Patients up to 25 years of age with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)<br><br>Relapsed or refractory large B-cell lymphoma<br><br>Relapsed or refractory follicular lymphoma (FL) | Dosing is based on the number of chimeric antigen receptor (CAR)-positive viable T cells.<br><br>**Pediatric and Young Adult B-cell ALL:**<br>Patients ≤50 kg: administer 0.2 to 5.0 x $10^6$ CAR-positive viable T cells per kg body weight via IV infusion<br><br>Patient >50 kg: administer 0.1 to 2.5 x $10^8$ total CAR-positive viable T cells (non-weight based) via IV infusion<br><br>**Adult Relapsed or Refractory Diffuse Large B-cell Lymphoma:**<br>0.6 to 6.0 x $10^8$ CAR-positive viable T cells via IV infusion<br><br>**Adult Relapsed or Refractory FL:**<br>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: 38225, 38226, 38227, 38228, 0870, 0871, 0872, 0873, 0874, 0875
For these codes, please assign the following revenue codes to the appropriate CPT codes:

- 0871 to CPT 38225
- 0872 to CPT 38226

- 0873 to CPT 38227
- 0874 to CPT 38228

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
- Q2054 – Lisocabtagene maraleucel, up to 110 million autologous anti-CD19 CAR positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
- Q2055 – Idecabtagene vicleucel, up to 460 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
- Q2056 – Ciltacabtagene autoleucel, up to 100 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

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

1. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in children and young adults with Bcell lymphoblastic leukemia. *N Engl J Med*. 2018;378(5):439-448.
2. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. *N Engl J Med*. 2020;382:1331-42.

**Policy Implementation/Update Information:** Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

April 2025: Coding change (Aucatzyl): Added HCPCS code C9301 to dosing reference table effective 4/1/2025; deleted C9399 termed 3/31/2025.
January 2025v2: Criteria change: Added newly approved Aucatzyl to policy for treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) with corresponding criteria and associated dosing within FDA label reference table. For

Breyanzi, added new indications for adults with relapsed or refractory follicular lymphoma (FL) after two or more prior lines of systemic therapy, and for adults with relapsed or refractory mantle cell lymphoma (MCL) after at least two prior lines of systemic therapy, with corresponding criteria and associated dosing within FDA label reference table. For Tecartus, updated lymphodepleting chemotherapy regimen for ALL indication according to FDA label for clarity. Other minor adjustments made throughout policy and FDA label reference table for clarity with no change to policy intent.
January 2025: Coding change: Added the following supporting CPT codes effective 1/1/2025: 38225 replacing 0537T, 38226 replacing 0538T, 38227 replacing 0539T, and 38228 replacing 0540T. Deleted CPT codes 0537T, 0538T, 0539T, and 0540T termed 12/31/2024.
April 2024v2: Criteria change: For Abecma, expanded relapsed or refractory multiple myeloma indication to use after two or more prior lines of therapy from use after four or more prior lines of therapy per updated FDA label, and updated associated dosing within FDA label reference table. For Carvykti, expanded relapsed or refractory multiple myeloma indication to use after at least one prior line of therapy from use after four or more prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent, and in patients who are refractory to lenalidomide (Revlimid).
April 2024: Criteria change: Added new indication for Breyanzi for adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least two prior lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor, with corresponding criteria and associated dosing within FDA label reference table.
November 2022: Criteria update: Added indication for Breyanzi for relapsed/refractory large B-cell lymphoma after one line of therapy, and added associated dosing within FDA label reference table.
October 2022: Coding update: For Carvykti: Added HCPCS code Q2056 and description to dosing reference section effective 10/1/2022; deleted C9098, J3490, J3590, J9999 termed 9/30/2022.
August 2022: Criteria change: Added new indication for Kymriah for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy, with corresponding criteria and dosing table updates.
July 2022: Coding update: Added HCPCS code C9098 to dosing reference table for Carvykti effective 7/1/2022, deleted C9399 termed 6/30/2022.
June 2022: Coding update: Adjusted related CPT codes section for clarity to indicate specific revenue codes associated with specific CPT and/or HCPCS codes.
April 2022: Criteria change: Added new indication for Yescarta for adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy with corresponding criteria and dosing table updates.
March 2022: Criteria change: Added new to market product Carvykti with corresponding criteria for indication of multiple myeloma.
February 2022: Criteria change: Added the following codes as other related CPT codes: 0870, 0871, 0872, 0873, 0874, and 0875. Added ALL indication for Tecartus.
January 2022: Coding update: For Abecma: Added HCPCS code Q2055 and description to dosing reference section effective 1/1/2022, deleted C9081, J3490, J3590, and J9999 termed 12/31/2021.

October 2021: Coding update: For Breyanzi: Added HCPCS code Q2054 and description to dosing reference section effective 10/1/2021, deleted C9076, J3490, J3590, and J9999 termed 9/30/2021. For Abecma: Added HCPCS code C9081 to dosing reference table effective 10/1/2021, deleted C9399 termed 9/30/2021.
July 2021: Coding update: Added HCPCS code C9076 to dosing reference table effective 7/1/2021, deleted C9399 termed 6/30/2021.
June 2021: Criteria change: Removed criteria points regarding requirement of no active infection including hepatitis B, hepatitis C, and HIV.
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.