CAR-T Cell Therapy

Policy Number:	**M20180425008**
Effective Date:	**6/1/2018**
Sponsoring Department:	**Health Care Services**
Impacted Department(s):	**Health Care Services**

Type of Policy: ☒ Internal ☒ External

Data Classification: ☐Confidential ☐Restricted ☒Public

Applies to (Line of Business):

☐ Corporate (All)
☒ State Products, if yes which plan(s): ☒MediSource; ☒ MediSource Connect; ☒Child Health Plus ☒Essential Plan
☒ Medicare, if yes, which plan(s): ☒MAPD; ☐PDP; ☒ISNP; ☒CSNP
☒ Commercial, if yes, which type: ☒Large Group; ☒Small Group; ☒Individual
☒ Self-Funded Services *(Refer to specific Summary Plan Descriptions (SPDs) to determine any pre-authorization or pre-certification requirements and coverage limitations. In the event of any conflict between this policy and the SPD of a Self-Funded Plan, the SPD shall supersede the policy.)*

Excluded Products within the Selected Lines of Business (LOB)

N/A

Applicable to Vendors? Yes ☐ No☒

Purpose and Applicability:

To set forth Independent Health's clinical coverage guidelines for **Car-T Cell Therapy** utilizing **Kymriah (tisagenlecleucel)**, **Yescarta (axicabtagene ciloleucel), Tecartus (brexucabtagene autoleucel) Breyanzi (lisocabtagene maraleucel), Abecma (Idecabtagene Vicleucel)** or **Carvytki (ciltacabtagene autoleucel).**

Policy:

Background:

CAR-T Cell therapy, also known as chimeric antigen receptor therapy, draws on the immune system's natural fighting ability to attack cancer. CAR-T Cells are prepared from the patient's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure. The leukapheresis product is sent to the manufacturer where the mononuclear cells are enriched for T cells. The T cells are expanded in cell culture, washed and formulated into a suspension, which is then cryopreserved. The T cells are genetically engineered to produce receptors on their surface called CARs. These receptors allow the T cells to recognize and attach to a specific protein, or antigen, on tumor cells. This process may take many days but is typically complete within about 21 days. The product is then infused into the patient. The goal is for the engineered cells to further multiply in the patient's body, and with guidance from their engineered receptors, recognize and kill cancer cells that harbor the antigen on their surfaces.

Several CAR-T Cell therapies, Kymriah (tisagenlecleucel), Yescarta (axicabtagene ciloleucel), Tecartus (brexucabtagene autoleucel) Breyanzi (lisocabtagene maraleucel) Abecma (Idecabtagene Vicleucel) and Carvytki (ciltacabtagene autoleucel) have been approved by the Food and Drug Administration (FDA). Kymriah has been approved for refractory or relapsed B-cell precursor acute lymphoblastic leukemia. Yescarta has been approved for the treatment of relapsed or refractory large B-cell lymphoma after 2 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. Tecartus has been approved for the treatment of relapsed or refractory mantle cell lymphoma (MCL) in adults. Breyanzi has been approved for 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. Abecma (Idecabtagene Vicleucel) was approved for multiple myeloma. Carvytki (ciltacabtagene autoleucel) was approved for multiple myeloma.

In November 2023 the FDA announced it is investigating the identified risk of T cell malignancy with serious outcomes, including hospitalization and death, and is evaluating the need for regulatory action. The FDA stated "it has received reports of T-cell malignancies, including chimeric antigen receptor CAR-positive lymphoma, in patients who received treatment with BCMA- or CD19-directed autologous CAR T cell immunotherapies. Reports were received from clinical trials and/or postmarketing adverse event (AE) data sources". In April 2024, the FDA stated a Boxed Warning is warranted for the following products Abecma (idecabtagene vicleucel), Breyanzi (lisocabtagene maraleucel), Carvykti (ciltacabtagene autoleucel), Kymriah (tisagenlecleucel), Tecartus (brexucabtagene autoleucel) and Yescarta (axicabtagene ciloleucel) to highlight the serious risk of T cell malignancies. In addition, FDA has required related updates to other sections of the label (Warnings and Precautions, Postmarketing Experience, Patient Counseling Information and Medication Guide).

An evaluation of the peer-reviewed scientific literature, including but not limited to subscription materials, has provided Independent Health the basis for its medical necessity coverage outlined below.

Commercial, Medicare (in the absence of CMS guidance), Self-Funded: CAR-T Cell Therapy is covered utilizing the criteria below.

The prescriber will submit documentation of response to Kymriah, Yescarta, Tecartus, or Breyanzi within 3 months following therapy as a follow-up to the prior approval request. In addition to the criteria below, product specific dosage and/or frequency limits may apply in accordance with the U.S. Food and Drug Administration (FDA)-approved product prescribing information, national compendia, Centers for Medicare and Medicaid Services (CMS) and other peer reviewed resources or evidence-based guidelines. Independent Health may deny, in full or in part, reimbursement for utilization that does not fall within the applicable dosage and/or frequency limits.

NOTE: Independent Health considers all other uses of Kymria, Yescarta, Tecartus, Breyanzi Abecma or Carvytki experimental and investigational. Independent Health considers repeat administration of Kymria, Yescarta, Tecartus, Breyanzi, Abecma or Carvytki experimental and investigational because the effectiveness of this approach has not been established. Kymriah, Yescarta, Tecartus, Breyanzi, Abecma and Carvytki are available only through a Risk Evaluation and Mitigation Strategy (REMS) program to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. The member's medical records submitted for review for all conditions should document that the above medical criteria are met, including office visit notes that contain the relevant history and physical and prior cancer treatment history. For medical necessity review for members receiving CAR T Cell therapy as part of a clinical trial, please refer to the Independent Health Clinical Trial Policy.

MediSource, MediSource Connect, Child Health Plus and Essential Plan: CAR-T Cell Therapy is covered utilizing the criteria below.

Medicare Advantage: There is currently a National Coverage Determination for Car-T Cell therapy. Please refer to the link listed in the Reference section for Medicare Advantage coverage. Given absence of Medicare specific medical necessity criteria this policy will apply to Medicare advantage.

Clinical Indications

CAR-T Cell Therapy may be considered medically necessary for Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members for **ALL** of the following**:**

- **1 or more** of the following clinical indications:
    - Kymriah (tisagenlecleucel) as single agent therapy for the treatment of patients with refractory or second relapsed B-cell precursor **acute lymphoblastic leukemia (ALL)** when **ALL** of the following criteria are met:
        - The patient has been diagnosed with relapsed/refractory B-cell precursor acute lymphoblastic leukemia (ALL)
        - The patient is 25 years of age or younger
        - Patient does not have an active infection or inflammatory disorder
        - The patient has a confirmed **CD19** tumor expression
        - The patient has not previously been treated with gene therapy or Kymriah

- The patient does not have Philadelphia Chromosome positive (Ph+) ALL OR the patient has Philadelphia Chromosome positive (Ph+) ALL and they have tried and failed, is intolerant to, or has a contraindication to at least 2 tyrosine kinase inhibitors (TKI)
- The patient has been treated with 2 cycles of standard chemotherapy without a complete response or achieved a complete response and experienced multiple relapses following standard chemotherapy (at least 2 cycles)

- Kymriah as single agent therapy for the treatment of patients with relapsed or refractory (r/r) large B-cell lymphoma when **ALL** of the following criteria are met:
  - The patient has been diagnosed with **1 or more** of the following relapsed/refractory B-cell lymphomas:
    - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
    - High grade B-cell lymphoma
    - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
  - The patient is 18 years of age or older
  - Patient does not have an active infection or inflammatory disorder
  - The patient has a confirmed CD19 tumor expression
  - The patient has not previously been treated with gene therapy or Kymriah
  - The patient has experienced disease progression following a trial of two or more lines of systemic therapy
  - The patient does not have primary central nervous system (CNS) lymphoma
  - The patient does not have human immunodeficiency virus (HIV), active Hepatitis B or C, active uncontrolled infection or any autoimmune disease requiring immune suppression
- Yescarta (axicabtagene ciloleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - The patient has been diagnosed with relapsed/refractory B-cell lymphoma including **1 or more** of the following:
    - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
    - Primary mediastinal large B-cell lymphoma
    - High grade B-cell lymphoma
    - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
  - The patient is 18 years of age or older
  - Patient does not have an active infection or inflammatory disorder
  - The patient has not previously been treated with gene therapy or Yescarta
  - The patient has experienced disease progression following a trial of two or more lines of systemic therapy
  - Previous therapy included anthracycline chemotherapy agent and an anti-CD20 antibody
  - The patient does not have primary central nervous system (CNS) lymphoma

- Patient has not received prior anti-CD19 therapy, (e.g., blinatumomab, etc.) OR patient previously received anti-CD19 therapy and re-biopsy indicates CD-19 positive disease
- Patient has an ECOG performance status of 0-1
- The patient does not have human immunodeficiency virus (HIV), active Hepatitis B or C, active uncontrolled infection or any autoimmune disease requiring immune suppression

- Tecartus (brexucabtagene autoleucel) for treatment of mantle cell lymphoma is considered medically necessary when **ALL** of the following criteria are met:
  - Patient has relapsed or refractory disease
  - Patient has at least one measurable lesion
  - Patient must have received previous systemic therapy which included at least one agent from **ALL** of the following categories:
    - Bruton tyrosine kinase (BTK) inhibitor (e.g., ibrutinib, acalabrutinib, zanubrutinib)
    - Anti-CD20 monoclonal antibody (e.g., rituximab)
    - Anthracycline-OR bendamustine-containing chemotherapy
  - The patient is 18 years of age or older
  - Patient does not have an active infection or inflammatory disorder
  - The patient does not have primary central nervous system (CNS) lymphoma
  - Patient did not receive prior allogeneic hematopoietic stem cell transplantation (HSCT)
  - The patient does not have human immunodeficiency virus (HIV), active Hepatitis B or C, active uncontrolled infection or any autoimmune disease requiring immune suppression
- Tecartus (brexucabtagene autoleucel) for treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) is considered medically necessary when ALL of the following criteria are met:
  - Patient has not received prior anti-CD19 therapy, (e.g., blinatumomab, etc.) OR patient previously received anti-CD19 therapy and re-biopsy indicates CD-19 positive disease
  - Patient does not have CNS-3 disease or CNS-2 disease with neurological changes
  - **1 or more** of the following:
    - Patient has Philadelphia chromosome (Ph)-negative disease
    - Patient has Philadelphia chromosome (Ph)-positive disease AND the disease is tyrosine kinase inhibitor (TKI) intolerant OR refractory to at least two (2) different TKIs
- Breyanzi® (lisocabtagene maraleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - The patient has been diagnosed with **1 or more** of the following:
    - Relapsed or refractory large B-cell lymphoma
    - 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
- Follicular lymphoma grade 3B

- The patient is 18 years of age or older
- The patient has not previously been treated with gene therapy or Breyanzi
- Patient does not have a clinically significant active systemic infection or inflammatory disorder
- The patient has experienced disease progression following a trial of two or more lines of systemic therapy
- The patient does not have primary central nervous system (CNS) lymphoma

- Abecma (Idecabtagene Vicleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - The patient is 18 years of age or older
  - The patient has a diagnosis of multiple myeloma
  - Patient does not have an active infection or inflammatory disorder
  - The patient has measurable disease defined by **1 or more** of the following:
    - Serum monoclonal paraprotein (M-protein) level greater than or equal to 1 g/dL
    - Urine M-protein level greater than or equal to 200 mg per 24 hours
    - Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio
  - Individual has relapsed or refractory disease, defined as progression after four (4) or more lines of systemic therapy (which may or may not include therapy supported by hematopoietic stem cell transplant), AND prior therapy includes **ALL** of the following:
    - Anti-CD38 antibody (for example, isatuximab or daratumumab)
    - Proteasome inhibitor (for example, ixazomib, bortezomib, or carfilzomib)
    - Immunomodulatory drug (for example, thalidomide, pomalidomide, or lenalidomide)
  - Individual was refractory to the last treatment regimen
  - Individual has adequate bone marrow reserve defined by **ALL** of the following:
    - Absolute neutrophil count (ANC) ≥ 1000 cells/uL
    - Platelet count ≥ 50,000 cells/uL
  - Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
  - Individual is using as a one-time, single administration treatment
- Carvytki (ciltacabtagene autoleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - Individual is 18 years of age or older

- Individual has a diagnosis of multiple myeloma
- Individual has measurable disease defined by **1 or more** of the following:
  - Serum monoclonal paraprotein (M-protein) level more than or equal to 1 g/dL
  - Urine M-protein level greater than or equal to 200 mg per 24 hours
  - Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa ambda free light chain ratio
- **1 or more** of the following:
  - Individual has relapsed or refractory disease, defined progression after four (4) or more lines of systemic therapy (which may or may not include therapy supported by hematopoietic stem cell transplant)
  - Individual is double-refractory to proteasome inhibitor and immunomodulatory drug; AND prior therapy includes **ALL** of the following:
    - Anti-CD38 antibody (for example isatuximab or daratumumab)
    - Proteasome inhibitor (for example, ixazomib, bortezomib, or carfilzomib)
    - An immunomodulatory drug (for example, thalidomide, pomalidomide, or lenalidomide)
- Individual has adequate bone marrow reserve defined by **ALL** of the following:
  - Absolute neutrophil count (ANC) ≥ 1000 cells/u
  - Platelet count ≥ 50,000 cells/uL
- Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
- Individual does not have an active infection or inflammatory disorder
- Individual is using as a one-time, single administration treatment

- Documentation is provided from the provider that consent has been obtained related to adverse events of neurotoxicity and cytokinase release including that acknowledgement of complications have been discussed in detail with the patient

CAR-T Cell Therapy may be considered medically necessary for State Product members for **1 or more** of the following clinical indications**:**

- Kymriah (tisagenlecleucel) for a diagnosis of B-cell precursor ALL and **ALL** of the following:
  - The patient must be 25 years of age (up to the end of the 25th year) or younger
  - The ALL must be refractory or in second or later relapse
  - The hospital administering tisagenlecleucel is appropriately certified to do so. The list of currently authorized treatment centers may be viewed here: https://www.us.kymriah.com/treatment-center-locator/
- Kymriah (tisagenlecleucel) for a diagnosis of 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 in adults and **ALL** of the following:

- The patient is 18 years of age or older
- The hospital administering tisagenlecleucel is appropriately certified to do so. The list of currently authorized treatment centers may be viewed here: https://www.us.kymriah.com/treatment-center-locator/

- Yescarta (axicabtagene ciloleucel) for a diagnosis of large B-cell lymphoma, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma and **ALL** of the following:
  - The patient must be an adult (18 years, 0 months and above)
  - The large B-cell lymphoma must be relapsed or refractory after two or more types of systemic therapy
  - The hospital administering axicabtagene ciloleucel is appropriately certified to do so. The list of currently authorized treatment centers may be viewed here: https://www.yescarta.com/find-a-treatment-center/
- Breyanzi (lisocabtagene maraleucel) for a diagnosis of 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 and the patient must be an adult (18 years, 0 months and above)
- Abecma (Idecabtagene Vicleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - The patient is 18 years of age or older
  - The patient has a diagnosis of multiple myeloma
  - Patient does not have an active infection or inflammatory disorder
  - The patient has measurable disease defined by **1 or more** of the following:
    - Serum monoclonal paraprotein (M-protein) level greater than or equal to 1 g/dL
    - Urine M-protein level greater than or equal to 200 mg per 24 hours
    - Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio
  - Individual has relapsed or refractory disease, defined as progression after four (4) or more lines of systemic therapy (which may or may not include therapy supported by hematopoietic stem cell transplant), AND prior therapy includes ALL of the following:
    - Anti-CD38 antibody (for example, isatuximab or daratumumab)
    - Proteasome inhibitor (for example, ixazomib, bortezomib, or carfilzomib)
    - Immunomodulatory drug (for example, thalidomide, pomalidomide, or lenalidomide)
  - Individual was refractory to the last treatment regimen
  - Individual has adequate bone marrow reserve defined by ALL of the following:
    - Absolute neutrophil count (ANC) ≥ 1000 cells/uL
    - Platelet count ≥ 50,000 cells/uL

- Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
- Individual is using as a one-time, single administration treatment
- Documentation is provided from the provider that consent has been obtained related to adverse events of neurotoxicity and cytokinase release including that acknowledgement of complications have been discussed in detail with the patient

- Carvytki (ciltacabtagene autoleucel) is considered medically necessary when **ALL** of the following criteria are met:
  - Individual is 18 years of age or older
  - Individual has a diagnosis of multiple myeloma
  - Individual has measurable disease defined by **1 or more** of the following:
    - Serum monoclonal paraprotein (M-protein) level more than or equal to 1 g/dL
    - Urine M-protein level greater than or equal to 200 mg per 24 hours
    - Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa ambda free light chain ratio
  - **1 or more** of the following:
    - Individual has relapsed or refractory disease, defined progression after four (4) or more lines of systemic therapy (which may or may not include therapy supported by hematopoietic stem cell transplant)
    - Individual is double-refractory to proteasome inhibitor and immunomodulatory drug; AND prior therapy includes **ALL** of the following:
      - Anti-CD38 antibody (for example isatuximab or daratumumab)
      - Proteasome inhibitor (for example, ixazomib, bortezomib, or carfilzomib)
      - An immunomodulatory drug (for example, thalidomide, pomalidomide, or lenalidomide)
  - Individual has adequate bone marrow reserve defined by **ALL** of the following:
    - Absolute neutrophil count (ANC) ≥ 1000 cells/u
    - Platelet count ≥ 50,000 cells/uL
  - Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
  - Individual does not have an active infection or inflammatory disorder
  - Individual is using as a one-time, single administration treatment
  - Documentation is provided from the provider that consent has been obtained related to adverse events of neurotoxicity and cytokinase release including that acknowledgement of complications have been discussed in detail with the patient

NOT COVERED for any of the following:

- For Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members; Kymriah for treatment of patients with primary central nervous system lymphoma

- For Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members; Breyanzi for treatment of patients with primary central nervous system lymphoma
- For Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members; all other uses of Kymria, Yescarta, Tecartus, Breyanzi, Abecma or Carvytki other than those listed above, are considered experimental and investigational
- For Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members; repeat administration of Kymria, Yescarta, Tecartus, Breyanzi, Abecma or Carvytki is considered experimental and investigational
- For Commercial, Medicare (in the absence of CMS guidance), or Self-Funded members; reimbursement for utilization that does not fall within the applicable dosage and/or frequency limits in accordance with the U.S. Food and Drug Administration (FDA)-approved product prescribing information, national compendia, Centers for Medicare and Medicaid Services (CMS) and other peer reviewed resources or evidence-based guidelines
- For State product members; Yescarta (axicabtagene ciloleucel) for the treatment of patients with primary central nervous system lymphoma

Pre-Authorization Required? Yes ☒ No ☐

Pre-authorization is required for this service.

Definitions

Abecma (Idecabtagene Vicleucel) 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.

Acute lymphoblastic leukemia (ALL) also called acute lymphoblastic leukemia, is a cancer that starts from the early version of white blood cells called lymphocytes in the bone marrow. Leukemia cells usually invade the blood fairly quickly, spreading to other parts of the body, including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testicles.

B-cell lymphoma is a type of cancer that forms in B Cells. B-cell lymphomas may be either indolent or aggressive. Most B-cell lymphomas are non-Hodgkin lymphomas, varieties of which include Burkitt lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma, follicular lymphoma, and mantle cell lymphoma. Prognosis and treatment depend on type and stage of the cancer.

Breyanzi (lisocabtagene maraleucel) is a CD19-directed genetically modified autologous T cell immunotherapy 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.

CAR-T Cell Therapy is a type of treatment in which a patient's T cells from their own blood are changed in the laboratory, so they will attack cancer cells. A gene for a special receptor, also known as a chimeric antigen receptor (CAR) which binds to a certain protein on the patient's cancer cells is added in the laboratory. Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion.

Carvytki (ciltacabtagene autoleucel) 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 a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

CD19 is a protein coding gene. This gene encodes a cell surface molecule which assembles with the antigen receptor of B lymphocytes in order to decrease the threshold for antigen receptor-dependent stimulation.

Kymriah (tisagenlecleucel) is a CD19-directed genetically modified autologous T cell immunotherapy used in patients up to 25 years old who have acute lymphoblastic leukemia (ALL) which is either relapsing or refractory.

Mantle Cell Lymphoma (MCL) is a form of mature B cell non-Hodgkin lymphomas (NHL). The course of MCL is moderately aggressive and variable. Most patients with MCL have advanced stage disease at diagnosis (70 percent) and approximately 75 percent of patients initially present with lymphadenopathy.

Multiple myeloma is typically characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures.

Philadelphia Chromosome is an abnormality of chromosome 22 in which part of chromosome 9 is transferred to it. Bone marrow cells that contain the Philadelphia chromosome are often found in chronic myelogenous leukemia and sometimes found in acute lymphocytic leukemia.

Tecartus (brexucabtagene autoleucel) is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

Yescarta (axicabtagene ciloleucel) is a CD19-directed genetically modified autologous T cell immunotherapy 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, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

References

Related Policies, Processes and Other Documents
Clinical Trial Policy, Policy No. M011011296

Non-Regulatory references

American Cancer Society [web site]. What Is Acute Lymphocytic Leukemia? Last revised October 17, 2018. Available at: https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/what-is-all.html Accessed April 21, 2025

Axicabtagene clioleucel. Drug Information. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Ciltacabtagene autoleucel: Drug information. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Freedman AS, Aster JC. Mantle cell lymphoma: Epidemiology, pathobiology, clinical manifestations, diagnosis, and prognosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Freedman AS, Friedberg JW. Diffuse large B cell lymphoma (DLBCL): Suspected first relapse or refractory disease in medically-fit patients In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Freedman AS, Friedberg JW. Treatment of relapsed or refractory diffuse mantle cell lymphoma. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Genecards Human Gene Database [web site]. CD19 Gene. Available at: http://www.genecards.org/cgi-bin/carddisp.pl?gene=CD19 Accessed April 21, 2025

Hartmann J, Schüßler-Lenz M, Bondanza A. Clinical development of CAR T cells-challenges and opportunities in translating innovative treatment concepts. EMBO Mol Med. 2017 Sep;9(9):1183-1197.

Idecabtagene vicleucel: Drug information. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Larson RA. Treatment of relapsed or refractory acute lymphoblastic leukemia in adults. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Laubach JP. Multiple myeloma: Treatment of third or later relapse. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Lisocabtagene maraleucel: Drug information. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

Locke FL, Neelapu SS, Bartlett NL, et al. Phase 1 Results of ZUMA-1: A Multicenter Study of KTE-C19 Anti-CD19 CAR T Cell Therapy in Refractory Aggressive Lymphoma. Mol Ther. 2017 Jan 4;25(1):285-295.

National Cancer Institute at the National Institutes of Health [web site]. NCI Dictionary of Cancer Terms. B-cell lymphoma. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/b-cell-lymphoma Accessed April 21, 2025

National Cancer Institute at the National Institutes of Health [web site]. NCI Dictionary of Cancer Terms. CAR T-cell Therapy. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy Accessed April 21, 2025

National Cancer Institute at the National Institutes of Health [web site]. NCI Dictionary of Cancer Terms. Philadelphia Chromosome. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/philadelphia-chromosome Accessed April 21, 2025

National Cancer Institute at the National Institutes of Health [web site]. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Updated March 10, 2022. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells Accessed April 21, 2025

National Comprehensive Cancer Network [web site]. B-Cell Lympomas Version 5.2023 July 7, 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf Accessed April 21, 2025

National Comprehensive Cancer Network [web site]. Multiple Myeloma Version 3.2023 – December 8, 2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf Accessed April 21, 2025

National Comprehensive Cancer Network (NCCN) [web site]. Management of Immunotherapy-Related Toxicities. Version 1.2024 — December 7, 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf . Accessed April 21, 2025

Santomasso BD, Nastoupil LJ, Adkins S, et al. Management of Immune-Related Adverse Events in Patients Treated With Chimeric Antigen Receptor T-Cell Therapy: ASCO Guideline. J Clin Oncol. 2021 Dec 10;39(35):3978-3992. doi: 10.1200/JCO.21.01992. Epub 2021 Nov 1. Erratum in: J Clin Oncol. 2022 Mar 10;40(8):919. PMID: 34724386.

Tisagenlecleucel. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on July 11, 2023.)

United States Food and Drug Administration (FDA) [web site]. FDA Investigating Serious Risk of T-cell Malignancy Following BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies. Available at: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-investigating-serious-risk-t-cell-malignancy-following-bcma-directed-or-cd19-directed-autologous Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. FDA Requires Boxed Warning for T cell Malignancies Following Treatment with BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies . Available at: https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-requires-boxed-warning-t-cell-malignancies-following-treatment-bcma-directed-or-cd19-directed Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Abecma (idecabtagene vicleucel).04/16/2024 . Available at: https://www.fda.gov/vaccines-blood-biologics/abecma-idecabtagene-vicleucel Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Breyanzi (lisocabtagene maraleucel). Page last updated 03/18/2024 . Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/breyanzi-lisocabtagene-maraleucel Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Carvytki (ciltacabtagene autoleucel). Page updated 04/12/2024. Available at: https://www.fda.gov/vaccines-blood-biologics/carvykti Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Kymriah (tisagenlecleucel) Page Last Updated 04/25/2024 . Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/kymriah 706.htm Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. FDA approves tisagenlecleucel for adults with relapsed or refractory large B-cell lymphoma. Last Updated: 05/03/2018. Available at: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm606540.htm Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Tecartus Package Insert. Content current as of 04/25/2024 . Available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/tecartus-brexucabtagene-autoleucel. Accessed April 21, 2025

United States Food and Drug Administration (FDA) [web site]. Yescarta (axicabtagene ciloleucel). Page Last Updated04/25/2024 . Available at: https://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/ucm581222.htm Accessed April 21, 2025

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 Apr 2;382(14):1331-1342.

Regulatory References

Centers for Medicare and Medicaid (CMS) [web site]. National Coverage Determination (NCD) Chimeric Antigen Receptor (CAR) T-cell Therapy. Available at: https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=374&ncdver=1&keywordtype=starts&keyword=chimeric&bc=0 Accessed April 21, 2025

New York State Medicaid Update [web site]; Volume 34; Number 1; January 2018: p. 5. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2018/2018-01.htm Accessed April 21, 2025

New York State Medicaid Update [web site]; Volume 34; Number 5; May 2018: p. 4. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2018/may18_mu.pdf Accessed April 21, 2025

New York State Medicaid Update [web site]; Volume 33; Number 11; November 2017: p. 6. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2018/2018-01.htm#yescarta Accessed April 21, 2025

New York State Medicaid Update [web site]; Volume 37; Number 12; October 2021 p.1 Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2021/docs/mu_no12_oct21_pr.pdf Accessed April 21, 2025

New York State Department of Health, Division of Managed Care Response to Coverage Question (CovQuest). Email response. June 14, 2021.

This policy contains medical necessity criteria that apply for this service. Please note that payment for covered services is subject to eligibility criteria, contract exclusions and the limitations noted in the member's contract at the time the services are rendered.

Version Control

Signature / Approval on File? Yes ☒ No☐

Revision Date	Owner	Notes
9/1/2025	Health Care Services	Revised- Formatting only
8/1/2025	Health Care Services	Reviewed
8/1/2024	Health Care Services	Revised
1/1/2024	Health Care Services	Revised
9/1/2023	Health Care Services	Revised
10/1/2022	Health Care Services	Revised
11/1/2021	Health Care Services	Revised
4/1/2021	Health Care Services	Revised
1/1/2021	Health Care Services	Revised
9/1/2020	Health Care Services	Revised
10/1/2019	Medical Management	Revised
7/1/2019	Medical Management	Revised
8/1/2018	Medical Management	Revised