Yescarta (axicabtagene ciloleucel)

Summary

The Plan members who have certain types of treatment-resistant lymphoma or leukemia may be eligible for chimeric antigen receptor (CAR) T-cell therapy. CAR T-cell treatment involves genetically modifying an individual's white blood cells to specifically target the cancer cells in the body. This type of therapy is also known as adoptive immunotherapy. The process involves:

1. Collecting an individual's white blood cells (T-cells) from their blood.
2. Genetically modifying the T-cells in a lab to express CARs that target specific cancer cell antigens (like CD19).
3. Multiplying the number of these CAR T-cells.
4. Depleting the individual's existing immune system, often with chemotherapy.
5. Infusing the expanded CAR T-cells back into the individual.
   The modified CAR T-cells can then recognize and attack cancer cells expressing the targeted antigen. They may continue to multiply and remain in the body long-term, potentially guarding against cancer recurrence.

NOTE: This guideline does not address adoptive T-cell therapy for metastatic prostate cancer: Sipuleucel-T (Provenge™). For sipuleucel-T (Provenge™), please review the criteria outlined in MCG Sipuleucel-T (A-0661).

Definitions:

"AIDS" stands for Acquired Immunodeficiency Syndrome. It is a condition caused by the Human Immunodeficiency Virus (HIV), which attacks the immune system and weakens its ability to fight off infections and diseases. AIDS is considered the most advanced stage of HIV infection and is characterized by severe immune deficiency, leading to life-threatening opportunistic infections, cancers, and neurological disorders.

"Allogeneic Stem Cell Transplant" is a treatment where donor stem cells are harvested and transferred into those with cancer or disorders (after their own immune system has been depleted using chemotherapy or total body irradiation) to repopulate their entire bone marrow with healthy cells.

"Autologous Stem Cell Transplant" is similar to allogeneic stem cell transfer, except the individual's own stem cells are used instead of a matched donor.

"B-cell lymphomas" refer to a group of non-Hodgkin's lymphomas developing from cancerous white blood cells (specifically B-lymphocytes), often involving lymph nodes or other extranodal tissues. This group of lymphomas includes, but is not limited to, the following:

- Burkitt lymphoma
- Diffuse large B-cell lymphoma (DLBCL)
- Primary mediastinal B-cell lymphoma (PMBCL)
- Mantle cell lymphoma
- Marginal zone lymphomas
- Transformed follicular lymphoma

"CAR T-cell" or "Chimeric Antigen Receptor T-cell" therapy is a type of adoptive immunotherapy where an individual's white blood cells (specifically T-lymphocytes) are genetically engineered to specifically target the receptors on the cancer cells (CD19 receptor in the case of B-cell lymphomas and leukemias), B-cell maturation antigen (BCMA) or prostatic acid phosphatase (PAP) in the case of prostate cancer).

"CAR-T cell-related encephalopathy syndrome" (CRES) is another inflammatory immune response that can occur with CAR-T treatment and is treated in the same way as CRS.

"Cytokine release syndrome" (CRS) is an inflammatory immune response that may occur with CAR T-cell treatment. It often manifests as fever, hypotension, nausea, and other symptoms, and is an emergent condition that may require prompt treatment with tocilizumab (treatment binds to and inhibits IL-6 to reduce inflammatory and immune excessive response) and/or corticosteroids.

"ECOG score" (Eastern Cooperative Oncology Group) is a measure of an individual's general well-being and ability to participate in activities of daily living. The score ranges from 0 (fully active with restrictions) to 5 (dead) and is available at https://ecog-acrin.org/resources/ecog-performance-status.

"HHV8 (Human herpesvirus 8)", also known as Kaposi's sarcoma-associated herpesvirus (KSHV), is a virus that can cause several types of cancers including Kaposi sarcoma, primary effusion lymphoma, and multicentric Castleman disease.

"Leukemia" refers to a type of malignancy affecting the bone marrow and circulating cells in the bloodstream. Acute lymphoid leukemia (ALL) is one example.

"MALT" stands for mucosa-associated lymphoid tissue, which is a type of tissue found in various mucosal surfaces of the body.

"Metastatic Castrate-Resistant Prostate Cancer" is prostate cancer that has metastasized or spread outside of the pelvis. Castrate-resistant refers to the state of the cancer not responding to medications or systemic agents that typically inhibit progression by blocking hormonal signals.

"Relapsed" refers to a lymphoma or leukemia that had previously responded to treatment with remission, but has returned after a period since the last treatment.

"Refractory" refers to a lymphoma or leukemia that has not responded, has progressed, or has not achieved remission.

Medical Necessity Criteria for Authorization

The Plan considers a single dose of Yescarta (axicabtagene ciloleucel) medically necessary when ALL the following criteria are met:

1. Prescribed by or in consultation with a hematologist-oncologist; *AND*
2. The member has documented evidence of ALL of the following:
    a. The member is scheduled for and can safely undergo lymphodepleting therapy (including chemotherapy and/or total body irradiation) before CAR T-cell treatment; *and*
    b. The member has undergone screening and meets ALL of the following:
        i. No evidence of active Central Nervous System (CNS) involvement by malignancy; *or*
        ii. No evidence of active uncontrolled infection or inflammatory disorders; *or*
        iii. No evidence of history of allogeneic stem cell transplantation, active graft vs. host disease (GVHD); *or*
        iv. No evidence of previous treatment with Yescarta (axicabtagene ciloleucel) or any other CD19-targeted CAR T-cell therapy; *AND*
3. The facility and/or provider attests they are prepared for the potential occurrence of a serious adverse effect; *AND*
4. The member meets the medical necessity criteria for the applicable indication listed below:

B-cell Lymphomas:

Pediatric Aggressive mature B-Cell Lymphomas:

The Plan considers a single dose of Yescarta (axicabtagene ciloleucel) medically necessary when ALL the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; AND
6. The member is less than 18 years of age; *AND*
7. The member has a diagnosis of Primary mediastinal large B-cell lymphoma; *AND*
8. The member is prescribed Yescarta (axicabtagene ciloleucel) for consolidation/additional therapy if partial response achieved after therapy for relapsed or refractory disease (after use of ≥ 2 prior chemoimmunotherapy regimens).

Adult B-cell Lymphomas

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member is 18 years of age or older; *AND*
7. The member has ONE (1) of the following large B-cell lymphomas, under the following conditions:
    a. If the member has had prior treatment with first-line chemoimmunotherapy and has any of the following B-cell lymphoma subtypes:
        i. AIDS-related B-cell lymphomas; *or*
        ii. Diffuse large B-cell lymphoma (DLBCL); *or*
        iii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type); *or*
        iv. Other high-grade B-cell lymphomas; *or*
        v. Primary mediastinal large B-cell lymphoma; *or*
        vi. DLBCL arising (histologic transformation) from follicular lymphoma or nodal marginal zone lymphoma; *or*
        vii. The member meets ONE of the following HIV-related B-cell lymphomas:
            1. HHV-8 associated B-cell lymphoma; *or*
            2. HIV-related diffuse large B-cell lymphoma; *or*
            3. Primary effusion lymphoma; *or*
            4. Plasmablastic lymphoma; *or*
    b. If the member has had prior treatment with TWO or more (≥2) lines of systemic therapy and has any of the following B-cell lymphoma subtypes:
        i. AIDS-related B-cell lymphomas; *or*
        ii. Diffuse large B-cell lymphoma (DLBCL); *or*
        iii. DLBCL arising (histologic transformation) from follicular lymphoma or nodal marginal zone lymphoma; *or*
        iv. Follicular lymphoma; *or*
        v. Gastric MALT lymphoma; *or*
        vi. Non-gastric MALT lymphoma; *or*
        vii. The member meets ONE of the following HIV-related B-cell lymphomas:
            1. HHV-8 associated B-cell lymphoma; *or*
            2. HIV-related diffuse large B-cell lymphoma; *or*

3. Primary effusion lymphoma; *or*
4. Plasmablastic lymphoma; *or*

viii. Monomorphic post-transplant lymphoproliferative disorder (B-cell type); *or*
ix. Extranodal or nodal marginal zone lymphoma; *or*
x. Other high-grade B-cell lymphomas; *or*
xi. Primary mediastinal large B-cell lymphoma; *or*
xii. Splenic marginal zone lymphoma; *AND*

9. Documented evidence that the member meets ALL of the following if applicable:
    a. For members with CD20-positive tumors, previous chemoimmunotherapy regimens should have included an anti-CD20 monoclonal antibody (e.g., Rituxan or rituximab biosimilars), unless contraindicated; *and/or*
    b. For diffuse large B-cell lymphoma arising from follicular lymphoma (i.e., histological transformation) of ONE of the following:
        i. As additional therapy for transformed disease following partial response, no response, or progressive disease to initial therapy with anthracycline-based regimens; *or*
        ii. As additional therapy after multiple lines of prior therapies including ≥2 chemoimmunotherapy regimens for indolent disease prior to histologic transformation (treatment should have included at least one anthracycline-based regimen, unless contraindicated).

Length of Stay

Initial Inpatient Admission - Up to 7 days

Extension Stay Criteria

Additional inpatient hospital days after 7 days are medically necessary when:

1. The member has cytokine release syndrome (CRS); *or*
2. The member has neurotoxicity, CAR-T Related Encephalopathy Syndrome (CRES); *or*
3. The member has developed any adverse reaction continuing after infusion that include, but are not limited to, fever, hypoxia, hypotension, tachycardia, hypersensitive reactions, hypogammaglobulinemia, infections-pathogen unspecified, bleeding episodes, diarrhea, nausea, vomiting, headache, acute kidney injury, edema, and delirium; *or*
4. The member is not stable for discharge, as outlined in the general recovery course and discharge criteria in MCG General Recovery Care > Problem Oriented General Recovery Guidelines >Medical Oncology GRG (PG-ONC).

Experimental or Investigational / Not Medically Necessary

CAR T-cell therapy for any other indication is considered experimental, investigational, or unproven. Non-covered indications and contraindications include, but are not limited to, the following:

- Any lymphoma subtype not mentioned above, including primary CNS lymphoma and Mantle cell lymphoma; *or*
- Any leukemia; *or*
- Any other cancer type or condition not included in the Clinical Indications criteria above; *or*
- When any other newly diagnosed malignancy or other malignancy that is under active treatment or not currently in remission is present; *or*
- Members with an ECOG score of 3-4, as the efficacy and evidence for use in those with poor performance status is limited; *or*
- The member has any of the following:
    - Live vaccination within 6 weeks of planned treatment date; *or*
    - Current pregnancy; *or*

Applicable Billing Codes (HCPCS/CPT Codes)

Table 1:	
CPT/HCPCS Codes for Adult B-Cell Lymphomas considered medically necessary if criteria are met:	
Code	*Description*
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
96416	Chemotherapy administration, intravenous infusion technique; initiation of prolonged chemotherapy infusion (more than 8 hours), requiring use of a portable or implantable pump

96417	Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (List separately in addition to code for primary procedure)
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Table 2:	
ICD-10 diagnosis codes considered medically necessary for Adult B-Cell Lymphomas with Table 1 (CPT/HCPCS) codes if the criteria are met:	
Code	*Description*
B20	Human immunodeficiency virus [HIV] disease
C82.00	Follicular lymphoma grade I, unspecified siteFollicular lymphoma
C82.01	Follicular lymphoma grade I, lymph nodes of head, face, and neck
C82.02	Follicular lymphoma grade I, intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb
C82.06	Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I, spleen
C82.08	Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I, extranodal and solid organ sites
C82.10	Follicular lymphoma grade II, unspecified site
C82.11	Follicular lymphoma grade II, lymph nodes of head, face, and neck
C82.12	Follicular lymphoma grade II, intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II, spleen
C82.18	Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II, extranodal and solid organ sites
C82.20	Follicular lymphoma grade III, unspecified, unspecified site
C82.21	Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck

C82.22	Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III, unspecified, spleen
C82.28	Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa, unspecified site
C82.31	Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck
C82.32	Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa, spleen
C82.38	Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.50	Diffuse follicle center lymphoma, unspecified site
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb

C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma, spleen
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma, unspecified site
C82.61	Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma, spleen
C82.68	Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.80	Other types of follicular lymphoma, unspecified site
C82.81	Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma, spleen
C82.88	Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma, extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified, unspecified site
C82.91	Follicular lymphoma, unspecified, lymph nodes of head, face, and neck
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified, intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified, spleen

C82.98	Follicular lymphoma, unspecified, lymph nodes of multiple sites
C82.99	Follicular lymphoma, unspecified, extranodal and solid organ sites
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.390	Primary central nervous system lymphoma
C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites

C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C83.90	Non-follicular (diffuse) lymphoma, unspecified, unspecified site
C83.91	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97	Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C85.10	Unspecified B-cell lymphoma, unspecified site
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17	Unspecified B-cell lymphoma, spleen
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
Z85.72	Personal history of non-Hodgkin lymphomas

Table 3:	
CPT/HCPCS Codes for Pediatric Aggressive B-Cell Lymphomas - Primary Mediastinal Large B-Cell Lymphomas considered medically necessary if criteria are met:	
Code	*Description*
0537T	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day

0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
0540T	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous
96365 - 96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug)
96413 - 96417	Chemotherapy administration, intravenous infusion technique
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Table 4:	
ICD-10 diagnosis codes considered medically necessary for Pediatric Aggressive B-Cell Lymphomas - Primary Mediastinal Large B-Cell Lymphomas with Table 3 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites

Table 5:	
ICD-10 diagnosis codes considered experimental, investigational, or unproven:	
C83.10 - C83.19	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C83.70	Burkitt lymphoma, unspecified site
C83.71	Burkitt lymphoma, lymph nodes of head, face, and neck
C83.72	Burkitt lymphoma, intrathoracic lymph nodes
C83.73	Burkitt lymphoma, intra-abdominal lymph nodes
C83.74	Burkitt lymphoma, lymph nodes of axilla and upper limb
C83.75	Burkitt lymphoma, lymph notes of inguinal region and lower limb
C83.76	Burkitt lymphoma, intrapelvic lymph nodes
C83.77	Burkitt lymphoma, spleen
C83.78	Burkitt lymphoma, lymph nodes of multiple sites
C83.79	Burkitt lymphoma, extranodal and solid organ sites
C83.70- C83.79	Burkitt lymphoma

References

1. ACTEMRA(R) intravenous, subcutaneous injection, tocilizumab intravenous, subcutaneous injection. Genentech Inc (per FDA), South San Francisco, CA, 2021.
2. Axicabtagene: New Drugs: Australian Prescriber. December 2021 Volume 44 Number 6. Retrieved from: https://www.nps.org.au/assets/AP/pdf/December-44-6-32pp-v2.pdf

3. Bouchkouj N, Kasamon YL, de Claro RA, et al. FDA Approval Summary: Axicabtagene Ciloleucel for Relapsed or Refractory Large B-cell Lymphoma. Clin Cancer Res. 2019 Mar 15;25(6):1702-1708. doi: 10.1158/1078-0432.CCR-18-2743. Epub 2018 Nov 9.
4. Burstein DS, Maude S, Grupp S, et al. Cardiac profile of chimeric antigen receptor T cell therapy in children: A single-institution experience. Biol Blood Marrow Transplant. 2018; 24(8):1590-1595.
5. Chavez JC, Bachmeier C, Kharfan-dabaja MA. CAR T-cell therapy for B-cell lymphomas: clinical trial results of available products. Ther Adv Hematol. 2019;10:2040620719841581.
6. Denlinger, N., Bond, D., & Jaglowski, S. (2021). CAR T-cell therapy for B-cell lymphoma. Current Problems in Cancer, 100826.
7. El-Galaly, T. C., Cheah, C. Y., Kristensen, D., Hutchison, A., Hay, K., Callréus, T., & Villa, D. (2020). Potentials, challenges and future of chimeric antigen receptor T-cell therapy in non-Hodgkin lymphomas. Acta Oncologica, 59(7), 766-774. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32189546/
8. Elsawy M, Chavez JC, Avivi I, et al. Patient-reported outcomes in ZUMA-7, a phase 3 study of axicabtagene ciloleucel in second-line large B-cell lymphoma. Blood. 2022 Nov 24;140(21):2248-2260. doi: 10.1182/blood.2022015478.
9. Grupp S, Laetsch T, Buechner J, et al. Analysis of a global registration trial of the efficacy and safety of CTL019 in pediatric and young Adults with relapsed/refractory acute lymphoblastic leukemia (ALL). Blood. 2016; 128(22):221.
10. Halford, Z., Anderson, M. K., Bennett, L. L., & Moody, J. (2021). Tisagenlecleucel in Acute Lymphoblastic Leukemia: A Review of the Literature and Practical Considerations. Annals of Pharmacotherapy, 55(4), 466-479. Retrieved from: https://pubmed.ncbi.nlm.nih.gov/32762363/
11. Kaplan LD & Ai W. HIV-related lymphomas: Treatment of systemic lymphoma. UpToDate. Last updated March 15, 2021.
12. Kersten MJ, Qiao Y, Shah R, et al. Quality-Adjusted Time without Symptoms or Toxicity: Analysis of Axicabtagene Ciloleucel versus Standard of Care in Patients with Relapsed/Refractory Large B Cell Lymphoma. Transplant Cell Ther. 2023 May;29(5):335.e1-335.e8. doi: 10.1016/j.jtct.2023.01.008. Epub 2023 Jan 14.
13. Kite Pharma, Inc. Authorized treatment centers for Yescarta (axicabtagene ciloleucel). Available at: https://www.yescarta.com/authorized-treatment-centers/. Accessed on April 17, 2020.
14. Kochenderfer JN, Dudley ME, Kassim SH, et al. Chemotherapy-refractory diffuse large B-cell lymphoma and indolent B-cell malignancies can be effectively treated with autologous T cells expressing an anti-CD19 chimeric antigen receptor. J Clin Oncol 2015; 33:540.
15. Kymriah [Product Information], Novartis Pharmaceuticals Corporation, East Hanover, NJ; May 2018. Available at: https://www.fda.gov/media/107296/download. Accessed on April 17, 2020.
16. Lamprecht M, Dansereau C. CAR T-Cell Therapy: Update on the State of the Science. Clin J Oncol Nurs. 2019;23(2):6-12.
17. Locke FL, Ghobadi A, Jacobson CA, et al. Long-term study and activity of axicabtagene ciloleucel in refractory long B-cell lymphoma (ZUMA-1): a single-arm, multicenter, phase 1-2 trial. Lancet Oncol. 2019; 20:21-42.
18. Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. N Engl J Med. 2022 Feb 17;386(7):640-654. doi: 10.1056/NEJMoa2116133. Epub 2021 Dec 11.
19. 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;25(1):285-295.
20. Locke FL, Rossi J, Xue X, et al. Abstract CT020: immune signatures of cytokine release syndrome and neurologic events in a multicenter registrational trial (ZUMA-1) in subjects with refractory diffuse large B cell lymphoma treated with axicabtagene ciloleucel (KTE-C19). In: Proceedings of the AACR Annual Meeting, 1–5 April 2017 Washington, DC.
21. Maude SL, Frey N, Shaw PA, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. N Engl J Med. 2014; 371(16):1507-1517.

22. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in children and young adults with B-Cell lymphoblastic leukemia. N Engl J Med. 2018; 378(5):439-448.
23. National Comprehensive Cancer Network. Dictionary. https://www.nccn.org/patients/resources/dictionary/default.aspx Accessed 1/25/2021.
24. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," Acute Lymphoblastic Leukemia. Version 4.2023 — February 05, 2024. Accessed 3/12/2024.
25. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," B-Cell Lymphomas. Version 1.2024 — January 18, 2024. Accessed 3/12/2024.
26. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," B-Cell Lymphomas. Version 2.2025 — February 10, 2025. Accessed 5/13/2025.
27. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," Pediatric Acute Lymphoblastic Leukemia. Version 4.2024 — February 07, 2024. Accessed 3/12/2024.
28. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)® Pediatric Aggressive Mature B-Cell Lymphomas Version Version 1.2023 — April 4, 2023. Accessed on 3/12/2024.
29. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)® Pediatric Aggressive Mature B-Cell Lymphomas Version Version 2.2025 — April 28, 2025. Accessed on 5/13/2025.
30. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," Management of Immunotherapy-Related Toxicities. Version 1.2024 — December 7, 2023. Accessed 3/12/2024.
31. National Comprehensive Cancer Network® (NCCN), "NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)," Management of Immunotherapy-Related Toxicities. Version 1.2025 — December 20, 2024. Accessed 5/13/2025.
32. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® (NCCN). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/index.asp. Accessed on April 17, 2020.
33. National Library of Medicine (U.S.). (2017, April -). A Phase 2 Multicenter Study of Axicabtagene Ciloleucel in Subjects With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma (ZUMA-5). Identifier: NCT03105336. https://clinicaltrials.gov/ct2/show/study/NCT03105336
34. Neelapu SS, Dickinson M, Munoz J, et al. Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial. Nat Med. 2022 Apr;28(4):735-742. doi: 10.1038/s41591-022-01731-4. Epub 2022 Mar 21.
35. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med 2017; 377:2531.
36. Ogbda N, Arwood NM, Bartlett NL, et al. Chimeric Antigen Receptor T-Cell Therapy. JNCCN. 2018;16(9). doi:https://doi.org/10.6004/jnccn.2018.0073
37. Ong MZ, Kimberly SA, Lee WH, et al. FDA-approved CAR T-cell Therapy: A Decade of Progress and Challenges. Curr Pharm Biotechnol. 2024;25(11):1377-1393. doi: 10.2174/0113892010257212231001082741.
38. Pongas, G., & Cheson, B. (2021). Recent advances in the management of patients with relapsed/refractory follicular lymphoma. Blood and Lymphatic Cancer: Targets and Therapy, 11, 55.
39. Schepisi G, Cursano MC, Casadei C, et al. CAR-T cell therapy: a potential new strategy against prostate cancer. Journal for ImmunoTherapy of Cancer 2019;7:258. doi: 10.1186/s40425-019-0741-7
40. Schuster SJ, Bishop MR, Tam C, et al. Sustained disease control for adult patients with relapsed or refractory diffuse large B-Cell lymphoma: an updated analysis of Juliet, a global pivotal phase 2 trial of tisagenlecleucel. Blood 2018; 132: 1684.

41. Schuster SJ, Svoboda J, Chong EA, et al. Chimeric Antigen Receptor T Cells in Refractory B-Cell Lymphomas. N Engl J Med 2017; 377:2545.
42. Sharma P, Kasamon YL, Lin X, Xu Z, Theoret MR, Purohit-Sheth T. FDA Approval Summary: Axicabtagene Ciloleucel for Second-Line Treatment of Large B-Cell Lymphoma. Clin Cancer Res. 2023 Nov 1;29(21):4331-4337. doi: 10.1158/1078-0432.CCR-23-0568.
43. Sharma P, King GT, Shinde SS, Purev E, Jimeno A. Axicabtagene ciloleucel for the treatment of relapsed/refractory B-cell non-Hodgkin's lymphomas. Drugs Today. 2018;54(3):187-198.
44. US Food and Drug Administration (FDA). FDA drug safety communication: FDA investigating serious risk of T-cell malignancy following BCMA-directed or CD19-directed autologous chimeric antigen receptor (CAR) T cell immunotherapies. https://www.fda.gov/safety/medical-product-safety-information/bcma-directed-or-cd19-directed-autologous-chimeric-antigen-receptor-car-t-cell-immunotherapies-fda. Published November 28, 2023.
45. Westin JR, Locke FL, Dickinson M, et al. Safety and Efficacy of Axicabtagene Ciloleucel versus Standard of Care in Patients 65 Years of Age or Older with Relapsed/Refractory Large B-Cell Lymphoma. Clin Cancer Res. 2023 May 15;29(10):1894-1905. doi: 10.1158/1078-0432.CCR-22-3136.
46. Westin JR, Oluwole OO, Kersten MJ, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma. N Engl J Med. 2023 Jul 13;389(2):148-157. doi: 10.1056/NEJMoa2301665. Epub 2023 Jun 5.
47. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma Inc; April 2022.
48. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma Inc; November 2022.
49. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma Inc; December 2023.
50. Zhang C, Kasi A. Chimeric Antigen Receptor (CAR) T-Cell Therapy. [Updated 2019 Feb 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan.

Clinical Guideline Revision / History Information

Original Date: 5/5/2020

Reviewed/Revised: 03/11/2021,12/01/2021, 03/17/2022, 3/23/2023, 3/21/2024, 5/29/2024, 01/01/2026