MEDICAL POLICY

Excellus
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Medical Policy Title	**Chimeric Antigen Receptor T-Cell (CAR-T) Therapy for Candidate Selection**
Policy Number	**7.02.11**
Current Effective Date	**April 15, 2026**
Next Review Date	**December 2027**

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

This policy only applies to an individual if the CAR-T therapy drug has first been approved by the Health Plan Pharmacy.

POLICY STATEMENT(S)

I. Chimeric antigen receptor T-cell (CAR-T) therapy is **medically appropriate** for carefully selected candidates after drug approval by the Health Plam pharmacy and **ALL** of the following criteria are met:

   A. Individual is using as a one-time treatment;

   B. Multidisciplinary team has evaluated the individual and recommends treatment (see policy guidelines for required documentation);

   C. Individual has adequate organ function with no significant deterioration in organ function expected within four (4) weeks after apheresis.

II. CAR-T therapy is **not medically necessary** for individuals that have had a recent allogeneic transplant unless specifically permitted by the product labeling.

RELATED POLICIES

Administrative Policy

AP-29 Cellular/Chimeric Antigen Receptor T-cell Therapy (CAR-T)

Pharmacy Policy

Pharmacy-103 Chimeric Antigen Receptor T Cell (CAR-T) Therapy

POLICY GUIDELINE(S)

I. Required documentation from the multidisciplinary team that includes the individual's eligibility and risk for CAR-T therapy should include:

   (*Based on FDA approved indications, additional testing and documentation may be necessary to support the use of the medication.)

   A. Place of Service (POS)

1. Outpatient admission;
2. If inpatient admission is being requested, include documentation explaining why outpatient services are not appropriate or sufficient for the individual's care;

B. Clinical Evaluation
1. Risk benefit analysis completed by treatment center;
2. Confirmation of diagnosis;
3. Identification of comorbidities;
4. Management of co-morbidities;
5. Current assessment of co-morbidities;
6. Consult notes (if applicable);

C. Psycho-Social Evaluation
1. Identification of stressors;

D. Performance Status
1. Karnofsky performance score;
2. Palliative Performance Scale (PPS) score); or
3. Eastern Cooperative Oncology Group (ECOG) performance status;

E. Lab Tests
1. CBC;
2. Metabolic profile;
3. Serologies: CMV, Hepatitis B and C;
4. HIV testing;

F. Cardiac Assessment
1. 12 Lead EKG;
2. Echo or Muga Scan;

G. Pulmonary Assessment
1. Chest x-ray;
2. Pulmonary function tests (PFTs) for high-risk for respiratory failure (COPD, emphysema, a-1-antritrypsin deficiency, hepatopulmonary syndrome, or significant smoking history);

H. Age-Appropriate Screening Tests
1. Please refer to the U.S Preventive Services Task Force (USPSTF) website for list of age-

appropriate screening guidelines. https://uspreventiveservicestaskforce.org/uspstf/ [accessed 2025 Sep 17]

DESCRIPTION

CAR T-cell therapy is a form of cancer immunotherapy that involves genetically engineered T-cells. CAR-T therapy is used to treat some types of recurrent blood cancers such as B-cell acute lymphoblastic leukemia (ALL), diffuse large B-Cell lymphoma, follicular lymphoma, high-grade B-cell lymphoma, mantle cell lymphoma, multiple myeloma and primary mediastinal large B-Cell lymphoma.

The process typically begins with the collection of an individual's white blood cells through leukapheresis. These cells are then activated and genetically modified usually via retroviral or lentiviral transduction to express a chimeric antigen receptor that targets cancer cells. Once engineered, the CAR T-cells are expanded to clinically effective quantities, undergo rigorous quality control testing, and are cryopreserved.

Commercial CAR T-cell products are manufactured at centralized facilities, requiring the transport of the individual's apheresis material to the manufacturing site and the final CAR T-cell product back to the treatment center. Before infusion, individuals typically receive lymphodepleting chemotherapy to optimize the immune environment for CAR-T-cell function. The therapy is administered as a single intravenous infusion. Several CAR T-cell products have received FDA approval for the treatment of specific types of hematological malignancies.

SUPPORTIVE LITERATURE

Haslam et al (2023) sought to estimate how many individuals in the U.S. with advanced or metastatic cancer are eligible for and likely to respond to CAR T-cell therapy, based on FDA-approved indications and clinical trial data. In 2017, approximately 2.7% of patients were estimated to be eligible for CAR T-cell therapy, with 2.0% potentially able to respond. By 2023, eligibility increased to 3.9%, with the highest rates seen in large B-cell lymphoma (2.5%) and the lowest in mantle cell lymphoma (0.1%). The estimated response rate also rose to 3.4% in 2023, again with large B-cell lymphoma showing the highest potential response (2.1%). Across pivotal trials, the median response rate was 66.4%, ranging from 25.5% to 98%. However, most approvals were based on single-arm studies using surrogate endpoints, with only two randomized trials demonstrating survival benefits. While CAR T-cell therapies show promising response rates, the overall proportion of eligible and responsive patients among those with advanced cancers remains relatively low.

Pasqui et al (2022) conducted a systematic review to assess the efficacy and safety of CAR T-cell therapy in patients with hematological malignancies. The review included seven parallel randomized controlled trials (RCTs) comparing CAR-T therapy to standard treatments, encompassing a total of 2,464 patients. However, only three trials focused on B-cell lymphomas had available outcome data at the time of analysis. The study found adverse events were frequent but not significantly different from those observed with standard therapies. Survival and progression-related outcomes were supported by low to very low certainty of evidence. Quality of life outcomes were not reported in the

available data. The authors concluded that current evidence is insufficient to support the routine use of CAR T-cell therapy outside of clinical trials or compassionate use settings.

CD19-directed CAR T-cell therapy has shown high initial response rates in children and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL), although relapse remains common.

Shah et al (2021) conducted a phase I trial using autologous CD19.28z CAR T-cells in 50 patients, evaluating both treatment response and long-term outcomes. Overall, 62% achieved complete remission (CR), with 90.3% of those being minimal residual disease (MRD)-negative. Patients who received fludarabine/cyclophosphamide (Flu/Cy) lymphodepletion had significantly better outcomes (69% CR) compared to alternative regimens (25%). Cytokine release syndrome (CRS) occurred in 70% of patients, with 18% experiencing severe cases; neurotoxicity was seen in 20%, but all resolved. The therapy was also effective in patients with central nervous system (CNS) involvement. Median overall survival (OS) for the full cohort was 10.5 months, but among those who underwent allogeneic hematopoietic stem cell transplant (alloHSCT) after achieving MRD-negative CR, median OS extended to 70.2 months, with a 5-year event-free survival (EFS) of 61.9% and a relapse rate of only 9.5%. All MRD-negative CR patients who did not receive alloHSCT relapsed. These findings support the use of sequential CD19.28z CAR T-cell therapy followed by alloHSCT for durable disease control in high-risk pediatric and young adult B-ALL patients, with Flu/Cy lymphodepletion showing superior efficacy and CAR T-cell therapy proving feasible even in cases with active CNS disease.

PROFESSIONAL GUIDELINE(S)

The National Institute for Health and Care Excellence (NICE) provides evidence-based guidance on FDA approved CAR-T treatments for bone marrow and blood cancers, including diffuse large B-cell lymphoma and B-cell acute lymphoblastic leukemia (see reference section for drug specific recommendations from NICE).

National Comprehensive Cancer Network guidelines for B-Cell Lymphomas V3.2025 states that “if patients intend to receive CAR T-cell therapy or CD3 x CD20 bispecific antibody therapy, bendamustine should be used with caution. Delay bendamustine until after CAR-T leukapheresis.”

Epperla et al (2023) reported the American Society for Transplantation and Cellular Therapy (ASTCT) Clinical Practice Guidelines for Transplantation and Cellular Therapies in Diffuse Large B Cell Lymphoma. The recommendations state:

- “CAR-T therapy (axi-cel or lisocel) as a standard of care option in DLBCL refractory to first-line chemoimmunotherapy or relapsed within 12 months of first-line chemoimmunotherapy (grade A recommendation).”
- “CAR-T therapy in patients with late relapse who have not achieved remission after second-line therapies (grade A recommendation).”
- “CAR-T therapy in those who are not eligible for autologous-HCT because of comorbidities or age regardless of the timing of relapse (grade B recommendation).”

- "Does not consider secondary CNS involvement a contraindication for administering CAR-T therapy (grade B recommendation)."

Dhakal et al (2022) reported the ASTCT Clinical Practice Recommendations for Transplantation and Cellular Therapies in Multiple Myeloma. The recommendations state:

- "The exact timing and sequencing of therapies like CAR-T in the context of stem cell transplantation and other therapies is not established yet."

Iqbal et al (2024) reported the Clinical Practice Recommendations for Hematopoietic Cell Transplantation and Cellular Therapies in Follicular Lymphoma (FL). This was a collaborative effort on behalf of the ASTCT and the European Society for Blood and Marrow Transplantation. The recommendations state:

- "The panel does not recommend consolidation with CAR T-cell therapy ineligible FL patients incomplete or partial remission after first line therapies, outside the setting of a clinical trial."
- "The panel does not recommend commercially available CAR T-cell therapy ineligible, relapsed (within less than 24 months from receiving chemotherapy and without evidence of histological transformation) FL patients who have achieved complete or partial remission after second line therapies."
- The panel recommends considering CAR T-cell therapy in eligible, relapsed FL patients who have relapsed after an autologous transplant and did not achieve complete or partial remission to most recent anti-lymphoma treatment.
- "The panel recommends CAR T-cell therapy as a treatment option for patients who did not achieve complete or partial remission after second or subsequent line therapies."
- "The panel recommends CAR T-cell therapy ineligible, relapsed FL patients who have relapsed after allogeneic transplant and are untreated or did not achieve complete or partial remission to most recent anti-lymphoma treatment."

Kharfan-Dabaja et al (2025) reported the ASTCT Clinical Practice Recommendations on the Role of Allogeneic Hematopoietic Cell Transplantation and CAR-T Therapy in Patients with Chronic Lymphocytic Leukemia. Th e recommendations state:

- "The panel recommends CAR T-cell therapy in CLL patients whose disease relapsed and/or was refractory to both a covalent BTK inhibitor and a BCL-2 inhibitor and either responded or did not respond to a noncovalent BTK inhibitor."
- "The panel recommends CAR T-cell therapy for CLL patients whose disease relapsed and/or was refractory to both a covalent BTK inhibitor and a BCL-2 inhibitor."
- "The panel recommends CAR T-cell therapy in CLL patients that relapse after an allo-HCT."

REGULATORY STATUS

For recommendations related to FDA-approved CAR-T therapies, refer to the National Institute for Health and Care Excellence (NICE), which provides evidence-based guidance on CAR-T treatments for bone marrow and blood cancers, including diffuse large B-cell lymphoma and B-cell acute lymphoblastic leukemia (see reference section for drug specific recommendations from NICE).

CAR T-cell therapies that have been approved by the FDA for the treatment of various hematologic malignancies can be found on Pharmacy Policy-103. Available from: https://provider.excellusbcbs.com/documents/d/global/chimeric-antigen-receptor-t-cell-car-t-therapy [accessed 2025 Nov 10]

Drugs

The United States Food and Drug Administration (FDA) is responsible for ensuring the safety, efficacy, and quality of drugs sold in the United States. This includes both prescription and over-the-counter medications. Refer to the FDA Drug website. Available from: https://www.fda.gov/drugs [accessed 2025 Nov 10]

The FDA maintains information for consumers and health professionals on new drug warnings and other safety information, drug label changes, and shortages of medically necessary drug products. Available from: Drug Safety and Availability | FDA [accessed 2025 Nov 10]

Vaccines, Blood, and Biologics

The United States Food and Drug Administration (FDA) regulates vaccines, blood and blood products, and biologics via the Center for Biologics Evaluation and Research (CBER) which ensures the safety, efficacy, and quality of these products. Refer to the FDA vaccines/blood/biologics website. Available from: https://www.fda.gov/vaccines-blood-biologics [accessed 2025 Nov 10]

The FDA maintains information for consumers and health professionals on vaccine, blood and biologics warnings and other safety information. Available from: Recalls (Biologics) | FDA [accessed 2025 Nov 10]

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
38225	Harvesting of blood-derived T lymphocytes
38226	Preparation for transport (e.g., cryopreservation)

Code	Description
38227	Receipt and preparation of CAR-T cells
38228	Administration of CAR-T cells

HCPCS Codes

Code	Description
	See Pharmacy Policy 103 for Applicable Drug Codes

ICD10 Codes

Code	Description
C83.30–C83.39	Diffuse large B-cell lymphoma (DLBCL) (code range)
C91.00–C91.02	Acute lymphoblastic leukemia (ALL) (code range)
C90.00–C90.02	Multiple myeloma (code range)
C86.6	Primary cutaneous CD30-positive T-cell proliferations
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
Z80.6	Family history of leukemia
Z80.7	Family history of other malignant neoplasms of lymphoid, hematopoietic and related tissues
Z85.72	Personal history of non-Hodgkin lymphomas
Z92.850	Personal history of Chimeric Antigen Receptor T-cell therapy
Z92.858	Personal history of other cellular therapy
Z92.859	Personal history of cellular therapy, unspecified
Z92.86	Personal history of gene therapy

REFERENCES

Amini L, et al. Preparing for CAR T cell therapy: patient selection, bridging therapies and

lymphodepletion. Nat Rev Clin Oncol. 2022 May;19(5):342-355.

Dhakal B, et al. ASTCT Clinical Practice Recommendations for Transplantation and Cellular Therapies in Multiple Myeloma. Transplant Cell Ther. 2022 Jun;28(6):284-293.

Epperla N, et al. ASTCT Clinical Practice Recommendations for Transplantation and Cellular Therapies in Diffuse Large B Cell Lymphoma. Transplant Cell Ther. 2023 Sep;29(9):548-555.

Haslam A, Hoeg TB, Prasad V. Estimation of eligibility for and response to CAR-T therapy in the United States. Blood Adv. 2024 Feb 27;8(4):1032-1036.

Iqbal M, et al. Clinical practice recommendations for hematopoietic cell transplantation and cellular therapies in follicular lymphoma: a collaborative effort on behalf of the American Society for Transplantation and Cellular Therapy and the European Society for Blood and Marrow Transplantation. Transplant Cell Ther. 2024 Sep;30(9):832-843.

Karmali R, et al. Double hit & double expressor lymphomas: a multicenter analysis of survival outcomes with CD19-directed CAR T-cell therapy. Blood Cancer J. 2025 Mar 26;15(1):43.

Kharfan-Dabaja MA, et al. Clinical practice recommendations on the role of allogeneic hematopoietic cell transplantation and chimeric antigen receptor t-cell therapy in patients with chronic lymphocytic leukemia on behalf of the American society for transplantation and cellular therapy. Transplant Cell Ther. 2025 Aug;31(8):494-504.

Lee DW, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019 Apr;25(4):625-638.

McKenna M, et al. Real-world evidence of the safety and survival with CD19 CAR-T cell therapy for relapsed/refractory solid organ transplant-related PTLD. Br J Haematol. 2023 Jul;202(2):248-255.

National Comprehensive Cancer Network (NCCN). [Internet]. Clinical practice guidelines in oncology. B-Cell Lymphomas. V.3.2025. 2025 Aug 18 [accessed 2025 Nov 10]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

National Institute for Health and Care Excellence [Internet]. Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies. Technology Appraisal Guidance [TA872]. Published: 28 February 2023. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/ta933

National Institute for Health and Care Excellence [Internet]. Axicabtagene ciloleucel for treating relapsed or refractory diffuse large B-cell lymphoma after first-line chemoimmunotherapy. Technology Appraisal Guidance [TA895]. Published: 7 June 2024. [accessed 2025 Nov 10]. Available at https://www.nice.org.uk/guidance/ta895.

National Institute for Health and Care Excellence [Internet]. Axicabtagene ciloleucel for treating relapsed or refractory follicular lymphoma. Technology Appraisal Guidance [TA894]. Published: 7 June 2024. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/ta894/chapter/1-Recommendations

National Institute for Health and Care Excellence [Internet]. Brexucabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people 26 years and over. Technology Appraisal Guidance [TA893]. Published: 7 June 2023. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/ta893

National Institute for Health and Care Excellence [Internet]. Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma. Technology Appraisal Guidance [TA677]: Published: 24 February 2021. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/ta677

National Cancer Institute. [Internet]. CAR T cells: engineering patients' immune cells to treat their cancers. Updated March 2022. [accessed 2025 Nov 10]. Available from: https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

National Institute for Health and Care Excellence Technology [Internet]. Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukemia in people aged 25 years and under. Technology Appraisal Guidance [TA933]. Published 15 May 2024. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/TA975/chapter/1-Recommendations.

National Institute for Health and Care Excellence [Internet]. Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies. Technology Appraisal Guidance [TA933]. Published: 29 November 2023. [accessed 2025 Nov 10]. Available from: https://www.nice.org.uk/guidance/ta933

Oluwole OO, et al. Chimeric antigen receptor t-cell therapy in the outpatient setting: an expert panel opinion from the American society for transplantation and cellular therapy. Transplant Cell Ther. 2024 Feb;30(2):131-142.

Pasqui DM, et al. CAR-T cell therapy for patients with hematological malignancies. A systematic review. Eur J Haematol. 2022 Dec;109(6):601-618.

Phina-Ziebin X, et al. Outcome of high-grade B-cell lymphoma compared with other large B-cell lymphoma after CAR-T rescue: a DESCAR-T LYSA study. Blood Adv. 2025 May 27;9(10):2500-2510.

Roddie C, et al. Obecabtagene autoleucel in adults with b-cell acute lymphoblastic leukemia. N Engl J Med. 2024 Dec 12;391(23):2219-2230.

Shah NN, et al. Long-Term Follow-Up of CD19-CAR T-Cell Therapy in Children and Young Adults With B-ALL. J Clin Oncol. 2021 May 20;39(15):1650-1659.

SEARCH TERMS

Adoptive cell therapy and adoptive cell immunotherapy

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

NCD - Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24) [accessed 2025 Nov 10]

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION	
Committee Approval Dates	
12/18/25	
Date	**Summary of Changes**
01/07/26	Policy edit; administrative policy #AP-29 added to the refer to policy section
12/18/25	New Policy