

Carvykti (ciltacabtagene autoleucel; cilta-cel)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Carvykti (ciltacabtagene autoleucel; cilta-cel) is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with relapsed or refractory multiple myeloma, who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide.

The Plan's members who have certain types of treatment-resistant lymphoma, leukemia, or multiple myeloma 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.

Definitions

“CAR T-cell” or “Chimeric Antigen Receptor T-cell” therapy is a type of adoptive immunotherapy where a patient’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).

“Multiple Myeloma” is a cancer of a type of white blood cells called plasma cells. It is associated with bone lesions as well as elevated calcium, anemia, and elevated creatinine. It also affects the bone marrow. While multiple myeloma and its associated symptoms are treatable, it is generally thought of as incurable.

“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.

“ECOG score” (Eastern Cooperative Oncology Group) is a measure of a patient’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>.

“Proteasome inhibitors” are a class of medications that block the action of proteasomes, which break down proteins. Examples include but are not limited to: bortezomib, carfilzomib, and ixazomib.

“Immunomodulatory agents” are medications that influence the function of the immune system. Examples include but are not limited to: thalidomide, lenalidomide, and pomalidomide.

“Anti-CD38 monoclonal antibody” treatments target a cell marker often expressed by myeloma cells. Examples include but are not limited to: daratumumab, isatuximab, and felzartamab.

Medical Necessity Criteria for Authorization

The Plan considers a single dose of Carvykti (ciltacabtagene autoleucl) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a hematologist-oncologist; *AND*
2. The member is 18 years or older; *AND*
3. The member has relapsed or refractory multiple myeloma (RRMM) meeting International Myeloma Working Group (IMWG) diagnostic criteria; *AND*
4. The member meets ONE of the following prior therapy criteria:
 - a. Has received at least one prior line of therapy, including an immunomodulatory agent and a proteasome inhibitor, *AND* is lenalidomide-refractory; *or*

- b. Has received at least three prior lines of therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent; *AND*
Examples of prior therapies
 - i. Anti-CD38 monoclonal antibody: Darzalex (daratumumab), Sarclisa (isatuximab).
 - ii. Immunomodulatory agent: lenalidomide (Revlimid), Pomalyst (pomalidomide), Thalomid (thalidomide).
 - iii. Proteasome inhibitor: bortezomib (Vemclade), Kyprolis (carfilzomib), Ninlaro (ixazomib).
5. IF criterion 4a is met, the member is refractory to lenalidomide, defined as meeting at least ONE of the following:
 - a. Progressive disease during treatment with lenalidomide-containing regimen; *or*
 - b. Progressive disease within 60 days of completion of a lenalidomide-containing regimen;
or
 - c. Intolerance to lenalidomide (e.g., grade 3 or 4 adverse events that do not resolve or recur despite dose reduction); *AND*
 6. The member has active/measurable disease defined by IMWG or NCCN or has non-secretory multiple myeloma, with at least ONE of the following parameters:
 - a. Serum M-protein greater or equal to (\geq) 1.0 g/dL; *or*
 - b. Urine M-protein \geq 200 mg/24 hours; *or*
 - c. Serum free light chain (FLC) assay \geq 10 mg/dL provided the serum FLC ratio is abnormal;
or
 - d. In case of non-secretory multiple myeloma, evidence of myeloma cells in the bone marrow biopsy; *AND*
 7. The member has documented disease progression per IMWG criteria within 12 months of starting most recent anti-myeloma therapy; *AND*
 8. The facility and/or provider attests they are prepared for the potential occurrence of a serious adverse effect; *AND*
 9. The member has undergone screening *AND* meets ALL of the following:
 - a. No active uncontrolled infection or inflammatory disorders; *or*
 - b. No use of live vaccines; *or*
 - c. Not pregnant.

Length of Stay

Initial Inpatient Admission (when applicable) - Up to 7 days

Extension Stay Criteria

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

1. Member has cytokine release syndrome (CRS); *or*
2. Member has neurotoxicity, CAR-T Related Encephalopathy Syndrome (CRES); *or*

3. 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. 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.

Exclusions include, but are not limited to, the following:

- 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 (defined as requiring treatment in the past 3 years); *or*
- Members with an ECOG score of 3-4, as the efficacy and evidence for use in members with poor performance status is limited; *or*
- Dosage is greater than 1×10^8 CAR-positive viable T cells per single infusion; *or*
- The member has any of the following:
 - Prior CAR T-cell targeted therapy treatment (even if for another malignancy); *or*
 - Any prior B-cell maturation antigen (BCMA)-targeted therapy; *or*
 - Any targeted therapy, gene therapy, cytotoxic therapy, proteasome inhibitor therapy, or investigational drug treatment within 14 days prior to planned apheresis; *or*
 - Any monoclonal antibody treatment within 21 days prior to planned apheresis; *or*
 - An immunomodulatory agent therapy within 7 days prior to planned apheresis; *or*
 - Received either of the following:
 - An allogeneic stem cell transplant within 6 months before apheresis. Members who received an allogeneic transplant must be off all immunosuppressive medications for 6 weeks without signs of graft-versus-host disease (GVHD); *or*
 - An autologous stem cell transplant 12 weeks before apheresis; *or*
 - Received a live vaccine within 6 weeks of the planned treatment date; *or*
 - Are currently pregnant, breastfeeding, or planning to become pregnant; *or*
 - Have an active, severe systemic infection, including but not limited to infections currently requiring IV antibiotics; *or*
 - Have uncontrolled central nervous system disease, including but not limited to brain metastases, positive cerebrospinal fluid (CSF) disease, seizure disorder, dementia, history of stroke, cerebellar disease, or autoimmune CNS disease; *or*
 - Have any of the following cardiac conditions:
 - New York Heart Association (NYHA) stage III or IV congestive heart failure; *or*

- Myocardial infarction or coronary artery bypass graft (CABG) 6 months prior to enrollment; *or*
 - History of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration; *or*
 - History of severe non-ischemic cardiomyopathy; *or*
 - Impaired cardiac function (LVEF <45%) as assessed by echocardiogram or multiple-gated acquisition (MUGA) scan (performed 8 weeks of apheresis); *or*
- Are on systemic corticosteroid therapy exceeding ≥ 70 mg of prednisone (or an equivalent dose of another corticosteroid) within 7 days prior to apheresis; *or*
- Lab values outside the following limits:
 - Hemoglobin < 8.0 g/dL
 - Platelets < 50,000/mm³
 - ANC < 750 cells/mm³
 - AST or ALT >3 times the upper limit of normal
 - Total bilirubin >2 times the upper limit of normal
 - Creatinine clearance <40 ml/min
 - Corrected serum calcium >12.5 mg/dL or free ionized calcium >6.5mg/dL.

Applicable Billing Codes (HCPCS/CPT Codes)

CPT/HCPCS Codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
Q2056	Ciltacabtagene autoleucel, up to 100 million autologous b-cell maturation antigen (bcma) directed car-positive t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous
38225	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
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
36511	Therapeutic apheresis; for white blood cells
ICD-10 codes considered medically necessary if criteria are met:	

<i>Code</i>	<i>Description</i>
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.11	Plasma cell leukemia in remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues
ICD-10 codes <i>not</i> considered medically necessary:	
<i>Code</i>	<i>Description</i>
C90.01	Multiple myeloma in remission
C90.21	Extramedullary plasmacytoma in remission
C90.31	Solitary plasmacytoma in remission

References

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