Oscar Clinical Guideline: Carvykti (ciltacabtagene autoleucel; cilta-cel) (CG067, Ver. 3)

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 chimeric antigen receptor (CAR) T-cell therapy for adults with relapsed or refractory multiple myeloma (RRMM) after four or more lines of prior therapy.

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 a patient'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 starts by filtering the white blood cells from the patient's blood. The filtered cells are then genetically modified to target the tumor receptors and expanded to a greater quantity. The patient's existing immune system is then depleted, often with chemotherapy, prior to infusion in order to allow for a more effective environment for the CAR T-cells to function.

As there are potentially serious side effects, treatment should only be performed when the benefits outweigh the risks, under the care of a licensed physician and in an inpatient facility that is certified to

administer CAR T-cell therapy. The facility must provide adequate inpatient monitoring during the infusion or extremely close outpatient monitoring with transplant or CAR T-cell experience. The facility must also have at least two doses of tocilizumab immediately available should a severe adverse reaction occur. Patients are also expected to be available and within appropriate proximity of the treatment location to be monitored for 4 weeks after treatment. Carvykti is available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI REMS.

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 autoleucel)** 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 had four or more prior lines of therapy, including ALL of the following:
    a. A proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib); ***and***
    b. An immunomodulatory agent (e.g., lenalidomide, pomalidomide); ***and***
    c. An anti-CD38 monoclonal antibody (e.g., daratumumab)***; AND***
5. The member has active/measurable disease defined by IMWG or NCCN or has non-secretory multiple myeloma, with the following parameters:
    a. Serum M-protein greater or equal to 1.0 g/dL; ***or***
    b. Urine M-protein greater or equal to 200 mg/24 h; ***or***
    c. Serum free light chain (FLC) assay greater or equal to 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***
6. The member has documented disease progression per IMWG criteria within 12 months of starting most recent anti-myeloma therapy***; AND***
7. The healthcare facility administering Carvykti is enrolled in the Carvykti Risk Evaluation and Mitigation Strategy (REMS) program***; AND***
8. The member has undergone screening and does NOT have any of the following:
    a. Active uncontrolled infection; ***or***
    b. Use of live vaccines; ***or***
    c. Pregnancy***; AND***
9. No contraindications (listed in "Experimental or Investigational / Not Medically Necessary" exclusions) are present**.**

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. Patient has cytokine release syndrome (CRS); *or*
2. Patient has neurotoxicity, CAR-T Related Encephalopathy Syndrome (CRES); *or*
3. Patient 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. Patient 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*
- Patients with an ECOG score of 3-4, as the efficacy and evidence for use in patients with poor performance status is limited; *or*
- Dosage is greater than 1×10^8 CAR-positive viable T cells per single infusion; *or*
- Any of the following contraindications:
    - 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 active HIV or Hepatitis B or C with a detectable viral load; *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 active autoimmune 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 5 mg/day of prednisone (or an equivalent dose of another corticosteroid) within 2 weeks prior to apheresis; *or*

- Lab values outside the following limits:
  - Hemoglobin < 8.0 g/dL
  - Platelets < 50,000/mm^3
  - ANC < 750 cells/mm^3
  - 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:	
Code	*Description*
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
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
36511	Therapeutic apheresis; for white blood cells
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved 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 *not* considered medically necessary:	
Code	*Description*
C90.01	Multiple myeloma in remission
C90.11	Plasma cell leukemia in remission
C90.21	Extramedullary plasmacytoma in remission
C90.31	Solitary plasmacytoma in remission

References

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Clinical Guideline Revision / History Information

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