STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Carvykti (ciltacabtagene autoleucel)
PAM-048

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	07/01/2022
Revision Number:	2	**Last Rev Date:**	10/20/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	10/18/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	01/20/2023

Overview

Medication:[1]	ciltacabtagene autoleucel
Brand Name:	Carvykti®
Pharmacologic Category:	B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy
FDA-Approved Indication(s):	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.
How Supplied:	Provided as a single dose for infusion containing a suspension of chimeric antigen receptor (CAR)-positive viable T cells in one infusion bag.
Dosage and Administration:	The recommended dose range is 0.5 – 1.0 $\times 10^6$ CAR-positive viable T cells per kilogram of body weight, with a maximum dose of 1×10^8 CAR-positive viable T cells per single infusion.
Benefit Category:	Medical

Black Box Warning

- **Cytokine Release Syndrome (CRS),** including fatal or life-threatening reactions, occurred in patients following treatment with Carvykti®. Do not administer to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS),** which may be fatal or life-threatening, occurred following treatment with Carvykti®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with Carvykti®. Provide supportive care and/or corticosteroids as needed.
- **Parkinsonism and Guillain-Barré syndrome and their associated complications** resulting in fatal or life-threatening reactions have occurred following treatment with Carvykti®.
- **Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS),** including fatal and life-threatening reactions, occurred in patients following treatment with Carvykti®. HLH/MAS can occur with CRS or neurologic toxicities.
- **Prolonged and/or recurrent cytopenias** with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with Carvykti®.
- **REMS program:** Carvykti® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI REMS.

Descriptive Narrative

Multiple myeloma (MM) is a malignant hematological disorder characterized by the clonal 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. Clinical manifestations of multiple myeloma may include bone pain, increased total serum protein concentration, anemia, hypercalcemia, and acute kidney failure.

MM primarily affects older individuals, the median age at diagnosis is 65 to 74 years. It is slightly more frequent in men than in women (approximately 1.4:1), and while MM occurs in all races and all geographic locations, the incidence varies by ethnicity. The incidence in African Americans and Black populations is two to three times that in White populations in studies from the United States and United Kingdom. In contrast, the risk is lower in the Japanese and Mexican populations.[2]

Data from the US Surveillance, Epidemiology, and End Results (SEER) registry estimates 35,730 new cases of MM and 12,590 deaths from MM in the United States in 2023 (representing 1.8% of all new cancer cases and 2.1% of all cancer deaths). This correlates with an annual incidence of 7.1 per 100,000 men and women per year, and a death rate of 3.2 per 100,000 men and women per year.

Most patients with multiple myeloma will have an initial response to treatment. However, conventional therapy is not curative, and MM will ultimately relapse. In addition, a minority will have primary refractory disease that does not respond to initial treatment. Relative survival is an estimate of the percentage of patients who would be expected to survive the effects of their cancer. It excludes the risk of dying from other causes. The introduction of proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, and stem cell transplantation has extended median survival.[3]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[4]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines for Multiple Myeloma (Version 1.2024 – September 22, 2023)[5]

NCCN Guidelines® Recommendation(s) for ciltacabtagene autoleucel in previously treated multiple myeloma
(1) Relapsed/refractory disease after 3 prior therapies [a,b] A. After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD [c] i. Idecabtagene vicleucel: Category 2A, preferred regimen PI = proteosome inhibitor IMiD = immunomodulatory drug [a] Regimens included under 1–3 prior therapies can also be used later in the disease course. Attempt should be made to use drugs/drug classes the patients have not been exposed to or exposed to >1 line prior. [b] Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT. [c] Patients can receive more than one B-cell maturation antigen (BCMA) targeted therapy, but optimal sequencing is unclear.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status[6]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Tocilizumab (Actemra®) may be required to manage cytokine release syndrome (CRS) or neurologic toxicities. HCPCS code J3262 suspends for claims review. If tocilizumab therapy is required, may be approved for up to 4 doses of 800 mg each.

Prior authorization is required.

Carvykti® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of multiple myeloma (MM); **AND**
2. Member is 18 years of age or older; **AND**
3. Member has relapsed or refractory disease after four or more prior therapies (which may or may not include therapy supported by hematopoietic stem cell transplant) **AND** prior therapy includes at least **ONE OF EACH** of the following categories:
    a. An immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide); **AND**
    b. A proteosome inhibitor (e.g., bortezomib, carfilzomib, ixazomib); **AND**
    c. An anti-CD38 monoclonal antibody (e.g., daratumumab, elotuzumab, isatuximab); **AND**
4. Member has a current Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1; **AND**
5. Prescribed by, or in consultation with, a hematologist or oncologist; **AND**
6. Member does not have active central nervous system involvement with MM: **AND**
7. Member has not received any previous treatment with B-cell maturation antigen (BCMA)-targeted therapy (e.g., Blenrep®, Tecvayli®); **AND**
8. Member has not received any previous treatment with chimeric antigen receptor (CAR) T-cell immunotherapy, e.g., Abecma®, Breyanzi®, Kymriah®, Tecartus®, or Yescarta®, nor will CAR T therapy or other genetically modified T-cell therapy be prescribed concurrently with Carvykti®; **AND**
9. Member is receiving Carvykti® as a one-time, single administration treatment; **AND**
10. Treatment will be administered at a facility that is certified under the Carvykti® Risk Evaluation and Mitigation Strategy (REMS) program; **AND**
11. Dose does not exceed 1×10^8 CAR-positive viable T cells.

Continued therapy will not be authorized, as Carvykti® is indicated to be dosed one time only.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization
Approval Duration	One course of treatment per lifetime	Not applicable.
Quantity Limits	One-time dose, not to exceed 1×10^8 CAR-positive T cells	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
~~C9098~~	~~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 *(effective 7/1/2022 – 9/30/2022)*~~
J3262	Injection, tocilizumab, 1 mg [Actemra®: may be required to manage cytokine release syndrome or neurologic toxicities]
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 *(effective 10/1/2022)*

ICD-10	Description
C90.0	Multiple myeloma
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
C90.02	Multiple myeloma in relapse

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
57894-0111-01	Janssen Biotech, Inc.	per treatment dose	1	EA	1
57894-0111-02	Janssen Biotech, Inc.	per treatment dose	1	EA	1

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Carvykti prescribing information (02/2023). Janssen Biotech, Inc.: Horsham, PA. Available online at www.carvyktihcp.com. Accessed August 24, 2023.

[2] Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. Connor RF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed October 10, 2023.

[3] SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. Available online at seer.cancer.gov/statfacts/html/mulmy.html. Accessed October 8, 2023.

[4] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed October 11, 2023.

[5] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.1.2024 – September 22, 2023. Accessed October 9, 2023. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guideline, go online to NCCN.org.

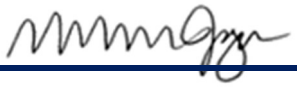
[6] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version

Signature

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Updated Descriptive Overview with 2023 statistics. Updated NCCN Guidelines. Removed criteria containing examples of measurable disease. Added criterion "Member has not received any previous treatment with B-cell maturation antigen (BCMA)-targeted therapy (e.g., Blenrep®, Tecvayli®)."	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
01/20/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee