Carvykti™ (ciltacabtagene autoleucel)
(Intravenous)

Document Number: IC-0663

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I. Length of Authorization

Coverage will be provided for one treatment course (1 dose of Carvykti) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 1 dose of up to 100 million autologous CAR-positive viable T-cells *(supplied as an infusion bag in a metal cassette)*

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit (1 dose of up to 100 million autologous CAR-positive viable T-cells)

III. Initial Approval Criteria [1,3]

Submission of medical records related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**
- Healthcare facility has enrolled in the CARVYKTI REMS Program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; **AND**
- Patient has not received prior CAR-T or B-cell maturation antigen (BCMA) targeted therapy; **AND**
- Patient has not received prior allogeneic hematopoietic stem cell transplant within 6 months prior to therapy; **AND**
- Patient does not have an active infection or inflammatory disorder; **AND**

- Patient has not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy, and will not receive live vaccines during ciltacabtagene autoleucel treatment, and until immune recovery following treatment; **AND**
- Patient has been screened for cytomegalovirus (CMV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
- Prophylaxis for infection will be followed according to standard institutional guidelines; **AND**
- Used as single agent therapy (not applicable to lymphodepleting or additional chemotherapy while awaiting manufacture); **AND**
- Patient does not have known central nervous system (CNS) involvement with myeloma or a history or presence of clinically relevant, active, CNS pathology; **AND**
- Patient does not have active or a history of plasma cell leukemia; **AND**
- Patient has an ECOG performance status of 0-1; **AND**

Multiple Myeloma † Φ [1-3]

- Patient has relapsed or refractory disease; **AND**
- Patient has received at least four (4) prior therapies, including a proteasome inhibitor (e.g., bortezomib, etc.), an immunomodulatory agent (e.g., lenalidomide, thalidomide, etc.) and an anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab, etc.)

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration [1]

Indication	Dose
Multiple Myeloma	<u>Lymphodepleting chemotherapy</u>: • Administer cyclophosphamide 300 mg/m^2 and fludarabine 30 mg/m^2 intravenously daily for three days. <u>Carvykti infusion</u>: • Infuse 2 to 4 days after completion of lymphodepleting chemotherapy. Delay the infusion up to 14 days if a patient has unresolved serious adverse events, active infections, or inflammatory disorders. • The recommended dose range is 0.5-1.0×10^6 CAR-positive viable T cells per kg of body weight, with a maximum dose of 1×10^8 CAR-positive viable T cells per single infusion.
For autologous use only. For intravenous use only. • Carvykti is prepared from the patient's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure. • One treatment course consists of lymphodepleting chemotherapy followed by an infusion of Carvykti.	

- Confirm Carvykti availability prior to starting the lymphodepleting regimen.
- Confirm the patient's identity with the patient identifiers on the shipper prior to infusion.

Premedication:

- Premedicate with 650 to 1000 mg acetaminophen and 25-50 mg diphenhydramine (equivalent) 30-60 minutes prior to infusion. Avoid prophylactic system corticosteroids which may interfere with Carvykti activity.

Monitoring after infusion:

- Monitor patients daily at a certified healthcare facility during the first ten days following infusion for signs and symptoms of CRS and neurologic toxicities.
- Monitor periodically for 4 weeks for signs and symptoms of delayed neurologic toxicity.
- Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.
- Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following infusion.

- Store infusion bag in the vapor phase of liquid nitrogen (less than or equal to minus 130°C). Thaw prior to infusion.
- In case of manufacturing failure, a second manufacturing may be attempted.
- Additional chemotherapy (not the lymphodepletion) may be necessary while the patient awaits the product.
- Ensure that 2 doses of tocilizumab and emergency equipment are available prior to infusion and during the recovery period.
- Carvykti contains human blood cells that are genetically modified with replication incompetent self-inactivating lentiviral vector. Follow universal precautions and local biosafety guidelines for handling and disposal.
- Do not use leukocyte depleting filters.

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drug
- C9399 – Unclassified drugs or biologicals (Hospital Outpatient Use) *(Discontinue use on 07/01/2022)*
- 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 07/01/2022)*

NDC:

- Carvykti suspension for intravenous infusion [A single dose of Carvykti contains a cell suspension of up to 1 x 10^8 CAR-positive T cells in one or more infusion bags]:
  - 30 mL and 70 mL infusion bags and metal cassettes: 57894-0111-xx

VII. References

1. Carvykti [package insert]. Horsham, PA; Janssen Biotech, Inc., March 2022. Accessed March 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ciltacabtagene autoleucel. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2022.
3. Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or

refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021 Jul 24;398(10297):314-324. doi: 10.1016/S0140-6736(21)00933-8. Epub 2021 Jun 24. Erratum in: Lancet. 2021 Oct 2;398(10307):1216.

4. Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant 2019; 25: 625-638
5. Majzner RG, Mackall CL. Tumor Antigen Escape from CAR T-cell Therapy. *Cancer Discov* 2018;8:1219-1226.
6. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood 2014; 124(2): 188-95. Errata in Blood: 2015;126(8):1048. and 2016;128(11):1533.
7. Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol 2016; 17(8): e328-46.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 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
D47.2	Monoclonal gammopathy
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Article and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC