MetroPlus Health

Policy and Procedure

Title: Carvykti (ciltacabtagene autoleucel)	Division: Medical Management Department: Utilization Management
Approval Date: 1/31/2023	LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, Goldcare I&II, Essential Plan, QHP
Effective Date: 1/31/2023	Policy Number: UM-MP346
Review Date: 1/30/2024	Cross Reference Number:
Retired Date:	Page 1 of 11

I. POLICY DESCRIPTION:

Medical Oncology – CAR-T immunotherapy, Carvykti (ciltacabtagene autoleucel)

II. RESPONSIBLE PARTIES:

Medical Management Administration, Utilization Management, Integrated Care Management, Pharmacy, Claim Department, Providers Contracting.

III. DEFINITIONS:

Carvykti (ciltacabtagene autoleucel) is an autologous chimeric antigen receptor T-cell (CAR-T) immunotherapy that genetically reprograms a patient's own T cells to have a chimeric antigen receptor (CAR), which will be able to identify and eliminate cancer cells that express an antigen called B-cell maturation antigen (BCMA). Carvykti is currently indicated for the treatment of adult patients with multiple myeloma that is refractory or is in relapse after using four or more lines of therapy including a proteasome inhibitor, immunomodulatory agent and an anti-CD38 monoclonal antibody.

IV. POLICY:

For the Medicare and UltraCare lines of business, MetroPlusHealth determines medical necessity based on applicable Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD).
https://www.cms.gov/medicare-coverage-database/search.aspx

For all non-Medicare LOBs:

Carvykti will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

INITIAL REQUEST:

1. **Multiple myeloma (MM) that is refractory or in relapse:**
   - **A.** Member is 18 years of age or older;
   - **AND**
   - **B.** Member has a diagnosis of relapsed or refractory multiple myeloma;
   - **AND**
   - **C.** Member has a measurable disease defined as ANY one of the following:
     - **a.** Serum monoclonal paraprotein (M-protein) ≥ 1 g/dL;
     - **OR**
     - **b.** Urine M-protein ≥ 200 mg/24 hours;

OR

c. Serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum free light chain ratio;

AND

D. Member has received treatment with at least four prior lines of therapy, including at least one drug from ALL of the following categories:

a. Proteasome inhibitor [e.g., bortezomib (Velcade), carfilzomib (Kyprolis)];

AND

b. Immunomodulatory agent [e.g., lenalidomide (Revlimid), pomalidomide (Pomalyst), thalidomide (Thalomid)];

AND

c. Anti-CD38 monoclonal antibody [e.g., daratumumab (Darzalex)];

AND

E. Member has an Eastern Cooperative Oncology Group (ECOG) score < 2;

AND

F. Member does not have a history or active central nervous system (CNS) involvement including signs of meningeal involvement of multiple myeloma;

AND

G. Member does not have an active inflammatory disorder;

AND

H. Member does not have ANY one of the following cardiac criteria:

a. New York Heart Association (NYHA) stage III or IV heart failure;

OR

b. Myocardial infarction or coronary artery bypass graft (CABG) in the last 6 months prior to Carvytki;

OR

c. Left ventricular ejection fraction (LVEF) < 45%;

OR

d. Significant ventricular arrhythmia or unexplained syncope;

OR

e. History of severe non-ischemic cardiomyopathy;

AND

I. Member meets ALL of the following lab criteria:

a. Absolute Neutrophil Count (ANC) ≥ 750 cells/mm^3;

AND

b. Platelet count ≥ 50,000/mm^3;

AND

c. AST/ALT does not exceed ≥ 3 times upper limit of normal;

AND

d. Member has a creatinine clearance ≥ 40 mL/min;

AND

J. Member does not have an active uncontrolled infection including human immunodeficiency virus (HIV), Hepatitis B or C and Cytomegalovirus (CMV);

AND

K. Member does not have any autoimmune disease requiring immunosuppression;

AND

L. Member does not have active or history of plasma cell leukemia;

AND

M. Member will not receive live vaccines 6 weeks prior to lymphodepleting chemotherapy and during administration of Carvykti and until immune recovery after treatment;

AND

N. Member has not received previous CAR-T therapy including Carvykti;

AND

O. Member has not used a previous therapy that targets BCMA;

AND

P. Carvykti will be prescribed through the consultation of a hematologist or oncologist;

AND

Q. Carvykti will be given accordingly based on the FDA approved dosing: One single intravenous dose ranging from 0.5-1.0 × 10^6 CAR-positive T cells/kg with a maximum dose of 1 × 10^8 CAR-positive T cells per single infusion to be given at least 2 days after completion of lymphodepleting chemotherapy;

AND

R. Member will receive Carvykti at a healthcare facility enrolled in the Carvykti REMS and are aware of how to manage Cytokine Release Syndrome (CRS) and neurological toxicities (See Appendices A and B)

Initial Duration of Approval: *One single dose per lifetime*

RENEWAL REQUEST:

Carvykti will not be renewed for additional requests as this is a single dose therapy.

Renewal Duration of Approval: *Not Applicable*

V. LIMITATIONS/ EXCLUSIONS:

- Carvykti is considered to be experimental and investigational if prescribed for indications other than for the treatment of multiple myeloma that is refractory or in relapse.
- Repeat infusions of Carvykti are considered to be experimental and investigational because there have been no established studies to demonstrate effectiveness.

VI. APPLICABLE PROCEDURE CODES:

CPT	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

VII. APPLICABLE DIAGNOSIS CODES:

CODE	Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse

VIII. REFERENCES:

1. Carvykti (ciltacabtagene autoleucel) [prescribing information]. Horsham, PA: Janssen Biotech, Inc; December 2023.
2. Janssen Research & Development, LLC. A Phase 1b-2, Open-Label Study of JNJ-68284528, A Chimeric Antigen Receptor T-Cell (CAR-T) Therapy Directed Against BCMA in Subjects With Relapsed or Refractory Multiple Myeloma. clinicaltrials.gov. Published April 21, 2022. https://clinicaltrials.gov/ct2/show/NCT03548207

IX. APPENDICES

Appendix A: CRS Grading and Management Guidance

CRS Grade	Tocilizumab	Corticosteroids**
Grade 1 Temperature 38 degrees C or higher*	If onset less than 72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).	--

<table>
<tr><td rowspan="2">Grade 2

Symptoms require and respond to moderate intervention.

Temperature 38 degrees C* with:

Hypotension not requiring vasopressors, and/or,

Hypoxia requiring oxygen via canula (low-flow nasal cannula is 6 L/min or lower; high-flow nasal cannula is greater than 6 L/min) or blow-by, or,

Grade 2 organ toxicity</td><td>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.

Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</td><td>Consider dexamethasone 10 mg IV every 12-24 hours.</td></tr>
<tr><td colspan="2">If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours).

If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg IV every 12 hours.

After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Monoclonal antibodies targeting cytokines may be considered depending on the institution practice for unresponsive CRS. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</td></tr>
<tr><td>Grade 3

Symptoms require and respond to aggressive intervention.

Temperature 38 degrees C or higher* with:</td><td>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.

Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</td><td>Administer dexamethasone 10 mg IV every 12 hours</td></tr>
</table>

Hypotension requiring 1 vasopressor with or without vasopressin, and/or, Hypoxia requiring oxygen via high-flow nasal canula (low-flow nasal cannula is 6 L/min or lower; high-flow nasal cannula is greater than 6 L/min), facemask, non-rebreather mask, or Venturi mask, or, Grade 3 organ toxicity or Grade 4 transaminitis.	If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours). If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg IV every 12 hours. After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Monoclonal antibodies targeting cytokines may be considered depending on the institution practice for unresponsive CRS. **Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.**	
Grade 4 Life-threatening symptoms. Requirements for ventilator support, continuous veno-venous hemodialysis (CVVHD). Temperature 38 degrees C or higher* with: Hypotension requiring multiple vasopressors (excluding vasopressin), and/or, Hypoxia requiring positive pressure (eg, CPAP, BiPAP, intubation, and mechanical	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. **Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.**	Administer dexamethasone 20 mg IV every 6 hours
	After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Monoclonal antibodies targeting cytokines may be considered depending on the institution practice for unresponsive CRS. **Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.** If no improvement within 24 hours, consider methylprednisolone (1-2 g IV, repeat every 24 hours if needed; taper as clinically indicated) or other immunosuppressants (e.g., other anti-T cell therapies).	

ventilation), or, Grade 4 organ toxicity (excluding transaminitis).	
*Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia, as it may be masked by interventions such as antipyretics or anti-cytokine therapy (eg, tocilizumab or steroids). Absence of fever does not impact CRS management decision. In this case, CRS management is driven by hypotension and/or hypoxia and by the more severe symptom not attributable to any other cause. **Continue corticosteroids use until the event is Grade 1 or less; taper steroids if total corticosteroid exposure is greater than 3 days.	

Appendix B: Neurologic Toxicity Grading and Management Guidance

ICANS GRADE^	Corticosteroids and Antiseizure Medications
Grade 1 Immune Effector Cell-Associated Encephalopathy (ICE) score 7 to 9*, or Depressed level of consciousness: awakens spontaneously	Consider dexamethasone 10 mg IV or equivalent every 12 to 24 hours for 2 to 3 days Start non-sedating, antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis.
Grade 2 ICE score 3 to 6*, or Depressed level of consciousness: awakens to voice	Administer dexamethasone 10 mg IV or equivalent every 12 hours for 2 to 3 days, or longer for persistent symptoms. Consider steroid taper if total corticosteroid exposure is greater than 3 days. If no improvement after 24 hours or worsening of neurologic toxicity, increase the dose and/or frequency of dexamethasone up to a MAX of 20 mg IV every 6 hours. Consider nonsedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis.

Grade 3 ICE score 0 to 2* (If ICE score is 0, but the patient is arousable (eg, awake with global aphasia) and able to perform assessment), or Depressed level of consciousness: awakens only to tactile stimulus, or Seizures, either: any clinical seizure, focal or generalized, that resolves rapidly, or non-convulsive seizures on EEG that resolve with intervention, or Raised intracranial pressure (ICP): focal/local edema on neuroimaging (intracranial hemorrhage with or without associated edema is not considered a neurotoxicity feature and is excluded from ICANS Grading)	Administer dexamethasone 10 to 20 mg IV or equivalent every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate dexamethasone or equivalent dose to at least 20 mg IV every 6 hours. Or escalate to high-dose methylPREDNISolone (1 to 2 g/day, repeat every 24 hours if needed; taper as clinically indicated). Consider nonsedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis. If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylPREDNISolone (1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated).
Grade 4 ICE score-0* (Patient is unarousable and unable to perform ICE assessment) or Depressed level of consciousness either: patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or stupor or coma, or Seizures, either: life-threatening prolonged seizure (longer than 5 minutes), or repetitive clinical or electrical seizures without return to baseline in between	Administer dexamethasone 20 mg IV or equivalent every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to high-dose methylPREDNISolone (1 to 2 g/day, repeated every 24 hours if needed; taper as clinically indicated). Consider nonsedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis. If raised ICP/cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylPREDNISolone (1 to 2 g/day, repeat every 24 hours if needed;

or motor findings**: deep focal motor weakness such as hemiparesis or paraparesis, or Raised intracranial pressure (ICP)/cerebral edema, with signs/symptoms such as: diffuse cerebral edema on neuroimaging, or decerebrate or decorticate posturing, or cranial nerve VI palsy, or papilledema, or Cushing' triad	taper as clinically indicated), and consider neurology and/or neurosurgery consultation.

^ICANS Grade and management is determined by the most severe event (ICE score, level of consciousness, seizure, motor findings, raised ICP/cerebral edema), not attributable to any other cause.
*If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, [eg, point to clock, pen, button = 3 points]); Following Commands (eg, "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point); and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.
**Tremors and myoclonus associated with immune effector cell therapies may be graded according to NCI CTCAE v5.0, but they do not influence ICANS Grading

MetroPlus Health

Policy and Procedure

Title: Carvykti (ciltacabtagene autoleucel)	**Division: Medical Management** **Department: Utilization Management**
Approval Date: 1/31/2023	**LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, Goldcare I&II, Essential Plan, QHP**
Effective Date: 1/31/2023	**Policy Number: UM-MP346**
Review Date: 1/30/2024	**Cross Reference Number:**
Retired Date:	**Page 10 of 11**

REVISION LOG:

REVISIONS	DATE
Creation date	1/2023
Effective	1/31/2023
Annual review	1/22/2024
Update LOBs to remove Medicare and Ultracare	8/12/2024

Approved: **Date:** David Ackman Digitally signed by David Ackman Date: 2024.08.29 12:44:30 -04'00'	**Approved:** **Date:** Sanjiv Shah MD Digitally signed by Sanjiv Shah MD Date: 2024.09.03 11:12:18 -04'00'
David Ackman, MD **VP of Medical Director**	**Sanjiv Shah, MD** **Chief Medical Officer**

Title: Carvykti (ciltacabtagene autoleucel)	Division: Medical Management Department: Utilization Management
Approval Date: 1/31/2023	LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, Goldcare I&II, Essential Plan, QHP
Effective Date: 1/31/2023	Policy Number: UM-MP346
Review Date: 1/30/2024	Cross Reference Number:
Retired Date:	Page 11 of 11

Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered andor paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members.
All coding and website links are accurate at time of publication.

MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.