BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 09/28/21**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 08/15/24**
	CURRENT EFFECTIVE DATE: 08/15/24
	LAST CRITERIA REVISION DATE: 08/15/24
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY FOR MULTIPLE MYELOMA

- **ABECMA® (idecabtagene vicleucel)**
- **CARVYKTI™ (ciltacabtagene autoleucel)**

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual is 18 years of age or older

  3. Individual has a confirmed diagnosis of **ONE** of the following:

     - **For Abecma**: Individual with relapsed or refractory multiple myeloma after **TWO or more** prior lines of therapy, including an immunomodulatory agent (e.g., lenalidomide, pomalidomide, or thalidomide), a proteasome inhibitor (e.g., bortezomib, carfilzomib, or ixazomib) and anti-CD38 monoclonal antibody (e.g., daratumumab or isatuximab)
     - **For Carvykti**: Individual with relapsed or refractory multiple myeloma after **ONE or more** prior lines of therapy, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, or ixazomib) and an immunomodulatory agent (e.g., lenalidomide, pomalidomide, or thalidomide), and are refractory to lenalidomide
     - Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. Individual does **NOT** have any of the following:

     - Active infection or inflammatory disease
     - Left ventricular ejection fraction less than 45%
     - Known active or prior history of significant central nervous system (CNS) disease, including CNS multiple myeloma
     - Active or prior history of plasma cell leukemia
     - Prior CAR T-cell therapy or any other gene therapy or is being considered for treatment with any other gene therapy
     - Live vaccines for at least 6 weeks prior to lymphodepleting chemotherapy and Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) treatment
     - Active graft versus host disease (GVHD)

  5. Individual with **ALL** of the following:

     - Eastern Co-operative Oncology Group (ECOG) performance status of 0-1
     - Negative pregnancy test (if individual is of childbearing potential)

- Has been screened for and treated as indicated for Hepatitis B, Hepatitis C, Cytomegalovirus (CMV) and human immunodeficiency virus (HIV)

Initial Approval:
One-time treatment infusion per lifetime for **ANY** CAR T-cell therapy treatment

Renewal Information:
Continued therapy will not be authorized for **ANY** CAR T-cell therapy treatment

- Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration.

Description:

Chimeric antigen receptor T (CAR-T) cells are a form of genetically modified autologous immunotherapy that can be directed at Multiple Myeloma (MM). This customized treatment uses the individual's own T lymphocytes, which are genetically modified (transfected) with a gene that encodes a chimeric antigen receptor to direct the individual's T cells against the MM cells. The T cells are genetically modified ex-vivo, expanded in a production facility, and then infused back into the individual as therapy. Prior to reinfusion, lymphodepleting chemotherapy regimen, cyclophosphamide plus fludarabine are administered.

Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) bind to BCMA-expressing target cells leading to CAR positive T cell proliferation, and elimination of BCMA BCMA-expressing cells. BCMA expression is largely restricted to plasma cells and is uniquely overexpressed on myeloma cells. Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) can persist in peripheral blood

for up to 1-year post infusion. Carvykti (ciltacabtagene autoleucel) may contain natural killer (NK) cells in addition to T cells.

Abecma (idecabtagene vicleucel) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after at least two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor and, and an anti-CD38 monoclonal antibody.

Carvykti (ciltacabtagene autoleucel) is indicated for the treatment of adult patients 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.

Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) have a Boxed Warning for Cytokine Release Syndrome (CRS), neurologic toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), and prolonged cytopenia with bleeding and infection, and t cell malignancies following CAR-T immunotherapies. Carvykti also has Boxed Warnings for Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), Parkinsonism, and Guillain-Barré syndrome and their associated complications. Individuals will be monitored for at least 7 days after Abecma (idecabtagene vicleucel) and for at least 10 days after Carvykti (ciltacabtagene autoleucel) at a REMS-certified healthcare facility for CRS and neurologic toxicities. The facility needs to have a minimum of 2 doses of tocilizumab and emergency equipment available prior to Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) infusion and during recovery period. . Additional monitoring for severe or life-threatening adverse events will be done for 4 weeks with supportive treatment as indicated.

Definitions:

Multiple Myeloma treatment options:

Immunomodulatory Agents	Proteosome Inhibitors	Anti-CD38 monoclonal antibodies
Lenalidomide Pomalidomide Thalidomide	Bortezomib Carfilzomib Ixazomib	Daratumumab Isatuximab

Risk Evaluation and Mitigation Strategy (REMS) Program:
Because of the risk of Cytokine Release Syndrome (CRS), the use of Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) are subject to a Risk Evaluation and Mitigation Strategy (REMS) programs called Abecma REMS and Carvykti REMS

The required components of the Abecma REMS and the Carvykti REMS:

- Healthcare facilities that dispense and administer ABECMA or Carvykti must be enrolled and comply with the REMS requirements.

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- Certified healthcare facilities must have on-site, immediate access to Tocilizumab.
- Ensure that a minimum of 2 doses of Tocilizumab are available for each patient for infusion within 2 hours after Abecma or Carvykti infusion, if needed for treatment of CRS.
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer ABECMA or Carvykti are trained in the management of CRS and neurologic toxicities.

ECOG Performance Status Table:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
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 housework, 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
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

History:	**Date**:	**Activity**:
Pharmacy and Therapeutics Committee	08/15/24	Review with revisions: criteria
Pharmacy and Therapeutics Committee	08/17/23	Reviewed with no revisions
Pharmacy and Therapeutics Committee	08/18/22	Review with revisions, new drug, coding, description, resources
Medical Policy Panel	09/28/21	Approved guideline
Clinical Pharmacist	09/03/21	Development

Coding:

HCPCS: Q2055, Q2056

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Resources:

Literature reviewed 08/15/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Abecma (idecabtagene vicleucel). Product information, revised by Celgene Corporation, and Bristol-Myers Squibb Company 04/2024, at DailyMed https://dailymed.nlm.nih.gov/dailymed/ Accessed July 8, 2024.

2. Carvykti (ciltacabtagene autoleucel injection) product information, revised by Janssen Biotech, Inc. 04/2024, at Daily Med https://daily med.nlm.nih.gov/dailymed/. Accessed July 8, 2024.

3. Laubach L. Multiple myeloma: Treatment of second or later relapse. In UpToDate, Rajkumar SV, Connor RF (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated June 14, 2024. Accessed July 8, 2024.

4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Multiple Myeloma Version 4.2024. Updated April 26, 2024. Available at: http://www.nccn.org. Accessed June 08, 2023.

5. Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

6. Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html