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# MEDICAL POLICY – 8.01.66

# Chimeric Antigen Receptor Therapy for Multiple Myeloma

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|---|---|---|
| BCBSA Ref. Policy: | 8.01.66 | |
| Effective Date: | Mar. 1, 2025 | RELATED MEDICAL POLICIES: |
| Last Revised: | Feb. 24, 2025 | None |
| Replaces: | N/A | |

**Select a hyperlink below to be directed to that section.**

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

## Introduction

Multiple myeloma (MM) is a cancer of a type of white blood cell known as a plasma cell. Normal plasma cells help the body fight infections. In multiple myeloma, abnormal plasma cells build up and reduce the body's ability to protect itself against infections. Multiple myeloma causes bone and calcium problems, low blood count, infections, and kidney problems. Chimeric antigen receptor (CAR) T-cell therapy is a type of treatment used for multiple myeloma that has either been treated and returned or that has continued to progress after previous treatment. In CAR T-cell therapy, specific immune system cells are withdrawn from the individual's blood, modified in a lab, and then given back to the individual. The goal of CAR T-cell therapy is for the modified immune cells to attack and destroy cancer cells. This policy describes when CAR T-cell drugs used to treat multiple myeloma may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

## Policy Coverage Criteria

| Drug | Medical Necessity |
|---|---|
| **Abecma (idecabtagene vicleucel) IV** | **Abecma (idecabtagene vicleucel) may be considered medically necessary for individuals with multiple myeloma when all the following criteria are met:**<br>• The individual is aged 18 years or older at the time of infusion<br>**AND**<br>• Has a documented diagnosis of multiple myeloma<br>**AND**<br>• Has relapsed or refractory disease after 2 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody (see Related Information)<br>**AND**<br>• Has adequate organ and bone marrow function as determined by the treating oncologist or hematologist<br>**AND**<br>• Does not have active infection(s) or inflammatory disorders<br>**AND**<br>• Has not received prior chimeric antigen receptor T therapy or any other gene therapy or are being considered for treatment with any other gene therapy<br><br>**Abecma is considered investigational when the above criteria are not met.** |
| **Carvykti (ciltacabtagene autoleucel) IV** | **Carvykti (ciltacabtagene autoleucel) may be considered medically necessary for individuals with multiple myeloma when all the following criteria are met:**<br>• The individual is aged 18 years or older at the time of infusion<br>**AND**<br>• Has a documented diagnosis of multiple myeloma<br>**AND**<br>• Has relapsed or refractory disease after 1 or more prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent (see Related Information)<br>**AND**<br>• Disease is refractory to lenalidomide<br>**AND** |

| Drug | Medical Necessity |
|---|---|
| | • Has adequate organ and bone marrow function as determined by the treating oncologist or hematologist<br>**AND**<br>• Does not have active infection(s) or inflammatory disorders<br>**AND**<br>• Has not received prior chimeric antigen receptor T therapy or any other gene therapy or are being considered for treatment with any other gene therapy<br><br>**Carvykti is considered investigational when the above criteria are not met.** |

| Drug | Investigational |
|---|---|
| **Abecma (idecabtagene vicleucel) IV, Carvykti (ciltacabtagene autoleucel) IV** | **The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**<br><br>**All other uses of Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) for conditions not outlined in this policy are considered investigational.** |

| Length of Approval | |
|---|---|
| **Approval** | **Criteria** |
| **Initial authorization** | **Non-formulary exception reviews for the drugs listed in this policy may be approved up to 12 months.**<br><br>**All other reviews for Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) may be approved as a one-time infusion.** |
| **Re-authorization criteria** | **Repeat treatment of Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) is considered investigational.** |

## Documentation Requirements

**The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:**

- Are adults (aged 18 years or older) at the time of infusion
- Have a documented diagnosis of multiple myeloma
- Have relapsed or refractory disease after prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
- Have adequate organ and bone marrow function as determined by the treating oncologist/hematologist
- Does not have active infection(s) or inflammatory disorders
- Have not received prior chimeric antigen receptor T therapy or any other gene therapy or are being considered for treatment with any other gene therapy.

# Coding

| Code | Description |
|---|---|
| **CPT** | |
| 0540T | Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous |
| **HCPCS** | |
| Q2055 | Idecabtagene vicleucel, up to 460 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose (use to report: Abecma) |
| 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 (use to report: Carvykti) |



# Related Information

## Benefit Application

Abecma (idecabtagene vicleucel) and Carvykti (ciltacabtagene autoleucel) are managed through the medical benefit.

## Consideration of Age

Age limits specified in this policy are determined according to the US Food & Drug Administration (FDA) approved indication.

## FDA Recommended Dose of Abecma (idecabtagene vicleucel) for Multiple Myeloma

300 to 460 x $10^6$ chimeric antigen receptor-positive viable T cells intravenously.

## FDA Recommended Dose of Carvykti (ciltacabtagene autoleucel) for Multiple Myeloma

0.5 to 1.0 x $10^6$ chimeric antigen receptor-positive viable T cells per kg of body weight with a maximum dose of 1 x $10^8$ chimeric antigen receptor-positive viable T cells per single infusion.

## Black Box Warning and Associated Restricted Program under a Risk Evaluation and Mitigation Strategy (REMS)

Abecma (idecabtagene vicleucel) has a black box warning because of the risks of cytokine release syndrome, neurologic toxicity, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, and prolonged cytopenia. Idecabtagene vicleucel should not be administered to individuals with an active infection or inflammatory disorders. It is recommended that severe or life-threatening cytokine release syndrome be treated with tocilizumab or tocilizumab and corticosteroids. Individuals should be monitored for neurologic events after treatment.

Abecma (idecabtagene vicleucel) is available only through a restricted program under a risk evaluation and mitigation strategy (REMS) called the Abecma REMS. The requirement for the REMS components are as follows:

- Health care facilities that dispense and administer this chimeric antigen receptor T therapy must be enrolled and comply with the REMS requirements.
- Certified health care facilities must have onsite, immediate access to tocilizumab, and ensure that a minimum of 2 doses of tocilizumab are available for each individual for administration within 2 hours after infusion of this chimeric antigen receptor T therapy, if needed for treatment of cytokine release syndrome.
- Certified health care facilities must ensure that health care providers who prescribe, dispense, or administer these chimeric antigen receptor T therapies are trained to manage cytokine release syndrome and neurologic toxicities.

## Black Box Warning and Associated Restricted Program under a Risk Evaluation and Mitigation Strategy (REMS) for Carvykti (ciltacabtagene autoleucel)

Carvykti (ciltacabtagene autoleucel) has a black box warning because of the risks of cytokine release syndrome, neurologic toxicity, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, and recurrent and prolonged cytopenia. Ciltacabtagene autoleucel should not be administered to individuals with an active infection or inflammatory disorders. It is recommended that severe or life-threatening cytokine release syndrome be treated with tocilizumab or tocilizumab and corticosteroids. Individuals should be monitored for neurologic events after treatment.

Parkinsonism and Guillain-Barré syndrome and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with Carvykti (ciltacabtagene autoleucel).

Carvykti (ciltacabtagene autoleucel) is available only through a restricted program under a REMS called the Carvykti REMS. The requirement for the REMS components are similar to the Abecma REMS.

## Guidance for Definitions for Relapsed and Refractory Multiple Myeloma

## Relapsed Multiple Myeloma

As per the 2016 International Myeloma Working Group Uniform Response Criteria for Multiple Myeloma, relapse requires 1 or more of the following direct indicators of increasing disease

and/or end organ dysfunction that are considered related to the underlying plasma cell proliferative disorder.

- Development of new soft tissue plasmacytomas or bone lesions
- Definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and at least 1 cm) increase as measured serially by the sum of the products of the cross-diameters of the measurable lesion
- Hypercalcemia (>11.5 mg/dL) [2.875 mmol/L]
- Decrease in hemoglobin of >2 g/dL [1.25 mmol/L] or to <10 g/dL
- Rise in serum creatinine by 2 mg/dL or more [177 µmol/L or more]
- Hyperviscosity

## Refractory Multiple Myeloma

In the protocol of the pivotal KarMMa and CARTITUDE-1 studies, refractory multiple myeloma was defined as documented progressive disease during or within 60 days (measured from the last dose) of completing treatment with the last anti-myeloma drug regimen. As per the 2016 International Myeloma Working Group Uniform Response Criteria for Multiple Myeloma, progression is defined as an increase of ≥25% from the lowest response value in any 1 or more of the following:

- Serum M-component (the absolute increase must be ≥0.5 g/dL) and/or
- Urine M-component (the absolute increase must be ≥200 mg/24 hour) and/or
- Only in subjects without measurable serum and urine M-protein levels: the difference between involved and uninvolved free light chains levels (the absolute increase must be >10 mg/dL)
- Only in subjects without measurable serum and urine M-protein levels and without measurable disease by free light chains levels: bone marrow plasma cell percentage (the absolute percentage must be ≥10%)
- Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas

- Development of hypercalcemia (corrected serum calcium >11.5 mg/dL) that can be attributed solely to the plasma cell proliferative disorder

## Prior Lines of Therapies for Multiple Myeloma

Three common classes of antimyeloma medications include anti-CD38 monoclonal antibodies (such as daratumumab or isatuximab), immunomodulatory drugs (such as thalidomide, lenalidomide, or pomalidomide) and proteasome inhibitors (such as bortezomib, carfilzomib, or ixazomib).

# Evidence Review

## Background

## Relapsed/Refractory Multiple Myeloma

Multiple myeloma is a hematologic malignancy characterized by the abnormal growth of plasma cells with production of abnormal proteins instead of typical antibodies. Plasma cell proliferation in the marrow causes bone pain and fractures due to lytic lesions and displaces other marrow cellular elements. The majority of individuals with myeloma present with symptoms related to organ involvement, including hypercalcemia, renal insufficiency, anemia, and bone lesions (known as calcium, renal failure, anemia, and bone lesions [CRAB] symptoms).[1]

Multiple myeloma is a relatively rare cancer with an annual incidence of approximately 7 in 100,000 Americans. It is estimated that 34,470 new cases of multiple myeloma were diagnosed in 2022, and 160,000 Americans are currently living with the disease.[2] The American Cancer Society estimated that there will be approximately 12,640 deaths in the United States in 2022.[3]

Multiple myeloma is primarily a disease of older adults, with a median age at diagnosis of 69. African Americans appear to be at approximately twice the risk of white Americans, while Asian-Americans appear to be at lower risk.[2] The risk for developing multiple myeloma is unusually high in individuals with a history of monoclonal gammopathy of undetermined significance, a benign presence of abnormal monoclonal proteins in the blood. Such individuals are likely to develop multiple myeloma or a related malignancy at a rate of 1% per year.[4]

## Diagnosis

Relapsed or refractory multiple myeloma is commonly identified through routine monitoring with laboratory studies using the standard 2016 International Myeloma Working Group response criteria for categorizing progression and relapse.[5] Progression is usually identified by a rise in monoclonal (M) protein in the serum or urine or in the serum free light chain ratio. Not all individuals with progression on laboratory testing need immediate treatment. Therapy is indicated if there is a clinical relapse, extramedullary disease, or a rapid rise in paraproteins.

## Current Treatment

The majority of individuals with multiple myeloma respond to initial therapies that consist of combination treatments and autologous stem cell transplant. However, conventional therapy is not curative and most of these individuals will ultimately progress. A small proportion of individuals do not respond to initial treatment (i.e., refractory disease).

There is no single standard treatment for individuals with relapsed/refractory multiple myeloma and multiple treatment options are used. Most individuals experience serial relapse and are treated with the majority of available agents at some point during their disease course. The main pharmacological medications used are monoclonal antibodies (daratumumab, elotuzumab, isatuximab), proteasome inhibitors (bortezomib, carfilzomib, ixazomib), immunomodulatory drugs (lenalidomide, pomalidomide, thalidomide), alkylators, anthracyclines, panobinostat, selinexor, and corticosteroids. A preferred order for their use has not been established. The choice of therapy at each relapse is informed by prior therapies used, response to these treatments, comorbidities, risk stratification, and the location of disease (e.g., extramedullary disease). Three-drug regimens are preferred over 2-drug regimens. However, 2-drug regimens are acceptable alternatives for frail individuals who may not be able to tolerate 3-drug regimens. According to the most recent NCCN clinical practice guideline (version 4, 2022), the triplet regimen including dexamethasone combined with a proteasome inhibitor, an immunomodulatory agent, or an anti-CD38 monoclonal antibody should be used as primary standard therapy for multiple myeloma (category 2A recommendation).[6]

Individuals with myeloma who have been treated with the 3 main backbones of interventional therapy (proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies) have poor outcomes to subsequent treatment. Individuals with heavily pretreated multiple myeloma that are daratumumab refractory have an expected median overall survival ranging from 6.6 to 9.3 months. Reported median progression-free survival for this population is 2.3 to 3.4 months.[7,8] In the observational MAMMOTH study, among participants with triple-class refractory

multiple myeloma on current therapies, the overall response rate was 31% with a median progression-free survival of 3.4 months.[8] Currently, belantamab mafodotin is the only US Food and Drug Administration (FDA) approved single agent treatment for individuals who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. Belantamab is an anti-B-cell maturation antigen (BCMA) humanized immunoglobulin G (IgG) antibody conjugated to an antineoplastic agent, monomethyl auristatin. This indication received an accelerated approval based on response rate and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. An overall response rate in the pivotal DREAMM-2 trial was achieved in 30 of 97 individuals studied (31%, 95% confidence interval [CI]: 21 to 43%). The median time to first response was 1.4 months (95% CI: 1.0 to 1.6) and 73% of responders had a duration of response ≥6 months.[9]

## Summary of Evidence

For individuals who are adults with relapsed and/or refractory multiple myeloma previously treated with 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody who receive idecabtagene vicleucel, the evidence includes one single-arm prospective trial. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The KarMMa study was a Phase 2, multicenter, open label study that enrolled adult individuals with relapsed or refractory multiple myeloma who received at least 3 different prior lines of therapy including proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies.

A FDA analysis included data from 100 individuals who received idecabtagene vicleucel in the dose range of 300 x $10^6$ and 450 x $10^6$. The primary end point was an overall response (partial response or better). After a median follow-up of 10.7 months, results showed an overall response rate of 72% and stringent complete responses in 28% of individuals. The median time to response was 30 days, and the median duration of response was 11 months, increasing to 19 months for individuals who achieved stringent complete responses. Minimal residual disease-negative status ($<10^{-5}$ nucleated cells) was achieved in 21% of all treated individuals and 75% of all individuals with a complete response or stringent complete response. In the absence of a randomized controlled trial (RCT), it is difficult to draw comparisons with currently available salvage treatment. Historically, in individuals with relapsed/refractory multiple myeloma who have disease progression despite receiving the three main classes of myeloma therapy, outcomes are poor. Complete responses are infrequent with reported median progression-free

survival ranging from 3 to 4 months, and a median overall survival of 8 to 9 months. With idecabtagene vicleucel, any grade cytokine release syndrome occurred in 85% of individuals, and grade ≥3 cytokine release syndrome occurred in 9% of individuals. Neurotoxicity occurred in 28% of individuals, reaching grade ≥3 severity in 4% of individuals. Notable limitations of the KarMMa study included lack of intention-to-treat analysis and a relatively short follow-up period to assess safety and efficacy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are adults with relapsed and/or refractory multiple myeloma previously treated with 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody who receive ciltacabtagene autoleucel, the evidence includes 1 single-arm prospective trial. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The CARTITUDE-1 study was a Phase 1b/2 multicenter open-label study that enrolled adult individuals with relapsed or refractory multiple myeloma who had received at least 3 different prior lines of therapy including proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies. The primary endpoint was overall response (partial response or better). After a median follow-up of 18 months, the primary efficacy analysis demonstrated an overall response rate of 98% (95 of 97) with a 78% rate of stringent complete response. In the absence of an RCT, it is difficult to draw comparisons with currently available treatments. Historically, in individuals with relapsed/refractory multiple myeloma who have disease progression despite receiving the 3 main classes of myeloma therapy, outcomes are poor. Complete responses are infrequent with reported median progression-free survival ranging from 3 to 4 months, and a median overall survival of 8 to 9 months. Notable adverse events of grade 3-4 among 97 individuals who received ciltacabtagene autoleucel included neutropenia (95%), anemia (68%), leukopenia (61%), thrombocytopenia (60%), and lymphopenia (50%). Any grade cytokine release syndrome and neurotoxicity were observed in 95% and 26% of individuals, respectively. Grade 3 to 4 cytokine release syndrome and neurotoxicity were observed in 5% and 11% of individuals, respectively. A notable limitation of the CARTITUDE-1 study included a relatively short follow-up period to assess safety and efficacy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

## Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in **Table 1**.

## Table 1. Summary of Key Trials

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| **Abecma (idecabtagene vicleucel)** | | | |
| **Ongoing** | | | |
| NCT04855136 (KarMMa-7) | Safety and Efficacy of bb2121 (Ide-cel) Combinations in Multiple Myeloma | 312 | Dec 2026 |
| NCT03601078 (KarMMa-2) | An efficacy and safety study of bb2121 in subjects with relapsed and refractory multiple myeloma and in subjects with high-risk multiple myeloma | 235 | Dec 2030 |
| **Unpublished** | | | |
| NCT02786511[a] | Long-term follow-up of subjects treated with bb2121 | 50 | Oct 2019 |
| NCT04196491 (KarMMa-4) | A study to evaluate the safety of bb2121 in subjects with high risk, newly diagnosed multiple myeloma | 13 | Dec 2023 |
| **Carvykti (ciltacabtagene autoleucel)** | | | |
| **Ongoing** | | | |
| NCT04133636 (CARTITUDE-2) | A study of JNJ-68284528, a CAR T-cell therapy directed against BCMA in participants with multiple myeloma | 237 | Nov 2028 |
| NCT04923893 (CARTITUDE-5) | A study of bortezomib, lenalidomide and dexamethasone (VRd) followed by Cilta-cel, a CAR T-cell therapy directed against BCMA versus VRd followed by lenalidomide and dexamethasone (Rd) therapy in participants with newly diagnosed multiple myeloma for whom ASCT is not planned as initial therapy | 743 | Jan 2034 |
| NCT05257083 (CARTITUDE-6) | A Study of Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) Followed by Ciltacabtagene Autoleucel Versus Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) Followed by Autologous Stem Cell Transplant (ASCT) in Participants With Newly Diagnosed Multiple Myeloma | 750 | Aug 2040 |
| NCT05201781 | A Long-term Study for Participants Previously Treated With Ciltacabtagene Autoleucel | 228 | Jul 2037 |

NCT: national clinical trial. [a] Denotes industry-sponsored or cosponsored trial.

## Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

## National Institute for Health and Care Excellence

### Idecabtagene Vicleucel

On November 30, 2023, the NICE issued a technology appraisal guidance [TA936] and stated that it is unable to make a recommendation on idecabtagene vicleucel for treating relapsed and refractory multiple myeloma after 3 or more treatments in adults because BMS did not provide a complete evidence submission.

### Ciltacabtagene Autoleucel

On May 17, 2023, the NICE issued a technology appraisal guidance [TA889] and stated that it is unable to make a recommendation on ciltacabtagene autoleucel (Carvykti) for treating relapsed or refractory multiple myeloma in adults because Janssen withdrew its evidence submission for the appraisal.

## Institute for Clinical and Economic Review

The Institute for Clinical and Economic Review (ICER) published an evidence report to assess the comparative clinical effectiveness and value of anti-B-cell maturation antigen CAR-T cell and antibody drug conjugate therapy for heavily pre-treated relapsed and refractory multiple myeloma.[17]

The ICER report notes that the evidence suggests that CAR-T cell therapies (idecabtagene vicleucel and ciltacabtagene autoleucel) for individuals with triple class refractory multiple myeloma likely provides small to substantial net health benefits over current usual care (Evidence rating B+). Benefits included longer survival as well as improved quality of life. Counterbalancing these benefits were the harms, including cytokine release syndrome, which is temporary but often requires hospitalization and intensive care unit level care. Further, the report concludes that the evidence is insufficient to determine whether 1 CAR-T therapy is

superior to the other. There are no studies comparing these agents directly, nor sufficient data to perform quantitative indirect comparisons.

## National Comprehensive Cancer Network

Current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for multiple myeloma (Version 1.2025 Sep 17, 2024) recommend (category 1) ciltacabtagene autoleucel as a treatment option for patients after one prior line of therapy including immunomodulatory agent and a proteasome inhibitor, and refractory to lenalidomide.

Current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for multiple myeloma (Version 1.2025 Sep 17, 2024) recommend (category 1) idecabtagene vicleucel as a treatment option for patients after two prior lines of therapy including immunomodulatory agent and a proteasome inhibitor.

## Medicare National Coverage

There is no national coverage determination.

## Regulatory Status

On March 26, 2021, idecabtagene vicleucel (Abecma) was approved by the FDA for the treatment of adult individuals with relapsed or refractory multiple myeloma after 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

On February 28, 2022, ciltacabtagene autoleucel (Carvykti) was approved by the FDA for the treatment of adult individuals with relapsed or refractory multiple myeloma after 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

## 2023 Update

Reviewed prescribing information for all drugs listed in policy. No new evidence found that would require changes in the policy statements.

## 2024 Update

Reviewed prescribing information for all drugs listed in policy. Clarified that Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) may be approved as a one-time infusion and repeat treatment is considered investigational. Updated Abecma (idecabtagene vicleucel) coverage criteria to include treatment of certain adults with multiple myeloma who have tried two prior therapies. Updated Carvykti (ciltacabtagene autoleucel) coverage criteria to include treatment of certain adults with multiple myeloma who have tried one prior therapy and lenalidomide.

## 2025 Update

Reviewed prescribing information for all drugs listed in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

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## History

| Date | Comments |
|---|---|
| 08/01/21 | New policy, approved July 13, 2021. Policy created with literature review through April 2, 2021. The use of Abecma (idecabtagene vicleucel) is considered medically necessary for individuals with relapsed and/or refractory multiple myeloma who have received four or more prior lines of therapy and when certain conditions are met. |
| 10/01/21 | Coding update, Added HCPC code C9081. |
| 1/1/22 | Coding update, Added HCPCS code Q2055. Removed HCPCS code J3590. |
| 10/01/22 | Annual Review, approved September 13, 2022. Policy updated with literature review through March 1, 2022. Relevant information on ciltacabtagene autoleucel for individuals with relapsed and/or refractory multiple myeloma was added. Ciltacabtagene autoleucel is considered medically necessary for adult individuals with relapsed and/or refractory multiple myeloma and have received four or more prior lines of therapy and when certain conditions are met. Changed the wording from "patient" to "individual" throughout the policy for standardization. Added HCPCS code Q2056. |
| 09/01/23 | Annual Review, approved August 7, 2023. Reviewed prescribing information for all drugs listed in policy. No new evidence found that would require changes in the policy statements. |
| 03/01/24 | Coding update. Added CPT code 0540T. |
| 04/01/24 | Annual Review, approved March 25, 2024. Clarified that Abecma (idecabtagene vicleucel) or Carvykti (ciltacabtagene autoleucel) may be approved as a one-time infusion and repeat treatment is considered investigational. |
| 07/01/24 | Interim Review, approved June 11, 2024. Updated Abecma (idecabtagene vicleucel) coverage criteria to include treatment of certain adults with multiple myeloma who have tried two prior therapies. Updated Carvykti (ciltacabtagene autoleucel) coverage criteria to include treatment of certain adults with multiple myeloma who have tried one prior therapy and lenalidomide. |
| 10/01/24 | Coding update. Added CPT codes 0537T-0539T to align with policy 8.01.63 Chimeric Antigen Receptor Therapy for Leukemia and Lymphoma. These codes are status B and are not billable separately. |
| 03/01/25 | Annual Review, approved February 24, 2025. Removed all status B codes from policy (0537T-0539T). There is a payment policy addressing all status B codes. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. |

**Disclaimer**: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. 

**Scope**: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.