Multiple myeloma (MM) is characterized by the expansion of malignant plasma cells in the bone marrow, resulting in an overabundance of monoclonal paraprotein (M protein), destruction of bone, and displacement of other hematopoietic cell lines. MM generally remains an incurable disease and most patients will eventually relapse following initial therapies and develop R/R MM. The depth and duration of response decrease with each successive treatment, as well as survival outcomes. MM accounted for approximately 1.8% (32,000) of all new cancer cases in the U.S. in 2020 with an overall 5-year survival rate estimated at 53% (ACS/Cancer Facts & Figures 2021; NCI/SEER 2020).

Relapsed/refractory MM (R/R MM) is defined as a disease which becomes non-responsive or progressive on therapy or within 60 days of the last treatment in patients who had achieved a minimal response or better on prior therapy. The mainstays of current MM treatment include three broad classes of drugs: immunomodulators, proteasome inhibitors, and monoclonal antibodies. However, patients who have tried the referenced drug classes (referred to as ‘triple-class exposed’) are unlikely to respond to further treatment attempts, have poor survival prospects and tend to demonstrate poor clinical outcomes with very low response rates (20% to 30%), short duration of response (2 to 4 months) (Kumar et al. 2012; Gandhi et al. 2019; Lonial et al. 2020). Most patients treated for R/R MM will continue to relapse and eventually develop disease refractory to immunomodulators, proteasome inhibitors, and monoclonal antibodies (Mihkael, 2020). Disease that is no longer responsive to each of these classes of treatments is referred to as “triple-class refractory” MM. Current approaches to the treatment of triple-class refractory disease are limited and include conventional chemotherapy, salvage autologous stem cell transplantation, and recycling previous regimens, each of which have generally had short-lived efficacy. There is no consensus on standard practice or regimen; a preferred order for conventional therapies has not been established and practice varies widely. Chimeric antigen receptor T-cell therapy (CAR T-cell therapy) against MM-associated antigens provides an additional option and promising positive response rates for patients with R/R MM.

CAR T-cell therapy are a form of immunotherapy in which immune cells are genetically engineered to target an antigen present on tumor cells so that they seek out those cells specifically; these T-cells then initiate an active and sustained immune response against the target cells (Skrabek, P et al. 2019). BCMA has been identified as a significant CAR target for treatment of MM since it is overexpressed on plasma cells but appears to be minimally expressed on other cells.

Abecma (idecabtagene vicleucel; ide-cel) is the first cell-based gene therapy approved for adults with MM and is a first-in class CAR-T cell therapy with BCMA-directed personalized immune cell therapy for relapsed or refractory MM patients. Ide-cel recognizes and binds to BCMA on the malignant plasma cells in MM, leading to the death of cancer cells. Abecma is delivered as a one-time infusion for triple-class exposed patients with MM. FDA approval was supported by results from the single-arm, multicenter, pivotal phase 2 KarMMa trial (NCT03361748), which evaluated the safety and efficacy of ide-cel in patients who had received at least 3 prior regimens for multiple myeloma and were refractory to their last regimen per International Myeloma Working Group (IMWG) criteria.
Abecma (ide-cel) for the treatment of relapsed or refractory multiple myeloma in adults may be considered medically necessary when ALL of the following clinical criteria are met:

1. Definitive diagnosis of multiple myeloma confirmed by bone marrow evaluation; **AND**
2. Member has measurable disease documented by at least ONE of following:
   a. Serum monoclonal paraprotein (M-protein) level greater than or equal to 1 g/dL; **OR**
   b. Urine M-protein level greater than or equal to 200 mg per 24 hours; **OR**
   c. Serum immunoglobulin free light chain greater than or equal to 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio.

**AND**

3. Relapsed or refractory disease after FOUR or more prior lines of therapy, including ALL of the following:
   a. Proteasome inhibitors [e.g., bortezomib (Velcade), carfilzomib (Kyprolis); ixazomib (Ninlaro)]; **AND**
   b. Immunomodulatory agents [e.g., lenalidomide (Revlimid), pomalidomide (Pomalyst), thalidomide (Thalomid)]; **AND**
   c. An anti-CD38 monoclonal antibody [e.g., daratumumab (Darzalex); elotuzumab (Empliciti), isatuximab (Sarcilisa)].

   **AND**
   d. Refractory to the most recently received therapy. Refractory disease defined as ≤ 25% response to, or progressing, during therapy within 60 days after last therapy.

**AND**

5. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; **AND**
   
   *Informational Note: KarMMa pivotal study*

6. Adequate bone marrow, cardiac, pulmonary, and organ function with no deterioration expected within 4 weeks after Abecma infusion, as determined by the treating oncologist/hematologist. Lab results must be submitted within 14 days of authorization confirming that member has adequate organ and bone marrow function.
   
   *Informational Note: While not a labeled contraindication, the KarMMa pivotal study excluded patients with a creatinine clearance of less than or equal to 45 mL/minute; alanine aminotransferase > 2.5 times upper limit of normal and left ventricular ejection fraction < 45%; and absolute neutrophil count < 1000 cells/mm$^3$ and platelet count <50,000/mm$^3$.**

**AND**

7. Clinical notes from member’s medical records, including: All relevant history and physical exams, disease staging, all prior therapies and cancer treatment history, anticipated treatment course applicable, labs and/or tests supporting the diagnosis (lab results must be dated within 14 days of request); **AND**

8. For member with a history of allogeneic stem cell transplant: Documentation (e.g., recent chart notes) confirming that member has no signs of active graft versus host disease (GVHD); **AND**

9. Confirmation/attestation of ALL of the following:
   
   a. Member will not receive ANY of the following:
      
      o A G-CSF agent within the first 3 weeks after Abecma infusion or until CRS has resolved; **AND**
      
      *Informational Note: Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and Abecma infusion. In the KarMMa study, 41% of patients (52/127) experienced prolonged Grade 3 or 4 neutropenia and 49% (62/127) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following Abecma infusion. In 83% (43/52) of patients who recovered from Grade 3 or 4 neutropenia after Month 1, the median time to recovery from Abecma infusion was 1.9 months.*
      
      o Live virus vaccine for at least 6 weeks prior to the start of lymphodepleting chemotherapy, **during** Abecma treatment and until immune recovery following treatment with Abecma.
AND

b. For members with a history of allogeneic stem cell transplant: Documentation (e.g., recent chart notes) confirming that member has no signs of active graft versus host disease (GVHD); **AND**

c. Member has not received, or is being considered for CAR-T therapy or other gene therapy; BCMA-targeted therapy; other investigational cellular therapy for cancer; **AND**

d. For women of reproductive potential:
   o Member is not pregnant or breast-feeding: Negative serum pregnancy test within the past 30 days; **AND**
   o Member has been counseled on the use of effective contraception during treatment.

CONTINUATION OF THERAPY

The safety and efficacy of repeat treatment has not been studied and is currently not supported by any compendia nor indicated in the current FDA approved labeling. Requests for reauthorization or beyond one dose is considered not medically necessary and will not be authorized.

Repeat administration of CAR-T cell is experimental and investigational since the safety and efficacy beyond one treatment has not been studied and is not indicated in the current FDA approval for Abecma. The evidence is insufficient to determine the effects on net health outcomes.

LIMITATIONS AND EXCLUSIONS

There are no contraindications listed in the manufacturer’s labeling at this time. The following are considered excluding based on insufficient evidence:

1. Prior treatment, or being considered for treatment, with CAR-T therapy or other gene therapy; OR repeat treatment with Abecma
2. Pregnancy: Not recommended for women who are pregnant, and pregnancy after Abecma infusion should be discussed with the treating physician
   **Informational Note:** It is not known if Abecma has the potential to be transferred to the fetus. Based on the mechanism of action, if the transduced cells cross the placenta, they may cause fetal toxicity, including B-cell lymphocytopenia and hypogammaglobulinemia.
3. Active hepatitis B virus (HBsAG positive) or active hepatitis C virus (anti-HCV positive) if viral load is detectable; Human immunodeficiency virus (HIV) positive.
   **NOTE:** A history of hepatitis B or hepatitis C is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing.
4. Active, uncontrolled infections (fungal, bacterial, viral, or other uncontrolled infections); Uncontrolled or requires IV antimicrobials (antibiotics, antifungals, antiprotozoals, antivirals)
5. Active inflammatory disorders
6. Active GVHD
7. Presence or history of:
   a. Plasma cell leukemia
   b. CNS involvement with myeloma
   c. Active or primary CNS disease; detectable cerebrospinal fluid malignant cells or brain metastases
   d. Primary CNS lymphoma or CNS disorder such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement
      **[Informational Note: NCCN guidelines define CNS involvement (CNS leukemia CNS-3) as the following: WBC count of ≥ 5 leukocytes/mcL in the CSF with the presence of lymphoblasts]**
8. History of class III or IV congestive heart failure (CHF) or severe non-ischemic cardiomyopathy, history of stroke, unstable angina, myocardial infarction, or ventricular arrhythmia within the previous 6 months.
9. Inadequate organ function
10. Ongoing treatment with chronic immunosuppressants
11. Second malignancies in addition to myeloma if the second malignancy has required therapy in the last 3 years or is not in complete remission.
12. Solitary plasmacytomas or non-secretory myeloma without other evidence of measurable disease.
The following are considered experimental, investigational and unproven based on insufficient evidence:

1. Any indications other than those listed above

   Based on the peer-reviewed medical literature the safety and effectiveness for indications other than the medically necessary indication listed above has not been established.

2. Prior treatment with any form of CAR T-cell therapy, or repeat administration of Abecma

DURATION OF APPROVAL: Duration sufficient for ONE single course of treatment.

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, an oncologist/hematologist at a certified treatment center.

AGE RESTRICTIONS: 18 years of age or older at time of infusion

Pediatric patients: The safety and efficacy of Abecma in patients under 18 years of age have not been established.

DOSING CONSIDERATIONS: A treatment course consists of lymphodepleting chemotherapy (consists of fludarabine 30 mg/m²/day and cyclophosphamide 300 mg/m²/day concurrently for 3 days) followed by Abecma infusion 2 days after completion of lymphodepleting chemotherapy. Confirm availability of autologous ide-cel prior to initiating lymphodepleting chemotherapy; AND

Abecma (IV infusion only): For autologous use only, administer 2-7 days after completing lymphodepleting chemotherapy; 300 to 460 × 10⁶ CAR-positive viable T-cells IV.

Premedication (acetaminophen and diphenhydramine) is required prior to ide-cel infusion. Ensure tocilizumab and emergency equipment are available prior to infusion and during recovery period.

MONITORING PARAMETERS:

- Monitor for signs/symptoms of Cytokine Release Syndrome (CRS), Neurologic Toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), and Prolonged Cytopenia [BOXED WARNINGS]

- Screen for hepatitis B virus (HBV), hepatitis C virus, and HIV in accordance with clinical guidelines prior to collection of cells for manufacturing. The American Society of Clinical Oncology HBV screening and management provisional clinical opinion (ASCO [Hwang 2020]) recommends HBV screening with hepatitis B surface antigen, hepatitis B core antibody, total Ig or IgG, and antibody to hepatitis B surface antigen prior to beginning (or at the beginning of) systemic anticancer therapy; do not delay treatment for screening/results. Detection of chronic or past HBV infection requires a risk assessment to determine antiviral prophylaxis requirements, monitoring, and follow-up.

QUANTITY LIMITATIONS:

ONE (1) single treatment course of Abecma per lifetime; AND

Concurrent Authorizations: Authorizations for Abecma will also receive approval of Actemra (tocilizumab). Max 8 single dose vials per lifetime [Refer to Actemra (tocilizumab) Policy No: C10265-A].

Informational Note: Actemra is indicated for the treatment of CAR T cell-induced severe or life-threatening CRS in patients ≥ 2 years of age. According to the FDA approved labeling for intravenous tocilizumab, the dose should not exceed 800 mg per infusion every 4 weeks for RA or CRS patients (Actemra Prescribing Information, 2020).

ADMINISTRATION:

1. Abecma is considered a provider-administered therapy under the expertise and safety measures available in certified treatment centers enrolled in the REMS program

   - 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 infusion, if needed for treatment of CRS.

   - Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer Abecma are trained on the management of CRS and neurologic toxicities.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: Intravenous Infusion

DRUG CLASS: Antineoplastic Agent, Anti-CD19; Antineoplastic Agent, Chimeric Antigen Receptor (CAR) T Immunotherapy; CAR-T Cell Immunotherapy; Cellular Immunotherapy, Autologous.

FDA-APPROVED USES: Multiple myeloma (MM), relapsed or refractory
Treatment of relapsed or refractory MM in adults after 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. FDA approval: March 26, 2021

COMPENDIAL APPROVED OFF-LABELED USES: None

RISK EVALUATION AND MITIGATION STRATEGY (REMS): Available only through the ABECMA REMS due to the serious risks of CRS and neurologic toxicities.

BOXED WARNING: CRS, Neurologic Toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), and Prolonged Cytopenia

SUMMARY OF MEDICAL EVIDENCE

FDA approval for Abecma (ide-cel) was based on data from the pivotal Phase 2 KarMMa study that evaluated its safety and efficacy in adults with R/R MM in North America and Europe (NCT03361748).
- The study met its primary endpoint of overall response rate and key secondary endpoint of complete response rate.
- Of 140 patients enrolled, 128 received Abecma. At a median follow-up of 13.3 months, 94 of 128 patients (73%) had a response, and 42 of 128 (33%) had a complete response or better. Minimal residual disease (MRD) negative status (<105 nucleated cells) was confirmed in 33 patients, representing 26% of all 128 patients who were treated and 79% of the 42 patients who had a complete response or better. The median progression-free survival was 8.8 months (95% confidence interval, 5.6 to 11.6).
- The efficacy evaluable population consists of 100 patients (n=100). Overall, 72 participants (72%) responded to Abecma and achieved a partial or complete response to treatment, including 44 whose tumors partially shrunk and 28 whose tumors disappeared completely (28%).
  - 28% of patients who had a complete response or remission (with disappearance of all signs of MM) and this was sustained by 65% of this group for at least 12 months.
  - Patients whose tumors disappeared completely stayed in remission for a median of 19 months.
  - For all participants who responded to the treatment, the remission lasted a median of 11 months.

KarMMa (Munshi et al., 2021)
- A pivotal, open-label, single-arm, multicenter, multinational, Phase 2 trial of 127 patients with R/R MM who received at least 3 previous regimens including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody. (Munshi et al., 2021)
- The efficacy evaluable population consists of 100 patients (n=100) who received Abecma within the dose range of 300 to 460 x 10⁶ CAR-positive T cells. Of these patients, 88% received four or more prior lines of therapy and 85% were triple-class refractory.
- Patient population included adult patients [median age of 61 years (age range 33-78); majority male (59%)] with
measurable disease; and adequate organ function.

- All enrolled patients had received at least 3 prior treatment regimens, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and were refractory to their last regimen, defined as progression during or within 60 days of their last therapy.
- The primary endpoint was overall response (partial response or better), defined according to IMWG Uniform Response Criteria for Multiple Myeloma.
- Key secondary endpoint is complete response rate. Other efficacy endpoints include time to response, duration of response, progression-free survival, overall survival, minimal residual disease.
- Primary and secondary end points were met.
- The overall response rate for the efficacy evaluable population (n=100) was 72% and 28% of patients achieved a stringent complete response.
- Responses were rapid and durable, with a median time to response of 30 days (range: 15 to 88 days) and median duration of response of 11 months for all responders and 19 months for those who achieved sCR. Of the 28 patients who achieved stringent complete response, an estimated 65% had remission lasting at least 12 months.
- The most common (≥ 20%) types of nonlaboratory adverse reactions included CRS, infections, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite.
- Serious adverse reactions occurred in 67% of patients, with the most common (≥5%) being CRS (18%), general physical health deterioration (10%), pneumonia (12%), infections (19%), viral infections (9%), sepsis (7%), and febrile neutropenia (6%). The most common Grade 3 or 4 nonlaboratory adverse reactions were febrile neutropenia (16%) and infections (14%). Fatal adverse reactions occurred in 6% of patients.
- Abecma carries a boxed warning for CRS, neurological toxicities, HLH/MAS, and prolonged cytopenia. Among 127 patients treated with ide-cel:
  - 85% of patients experienced low-grade CRS and 9% of patients had Grade 3 and higher CRS (only 1 patient had Grade 5 CRS)
  - CRS commonly occurred on day 1 and median time to resolve was 5 days
  - Neurotoxicity occurred in 28% of patients with 4% of patients having neurotoxicity over Grade 3; median time to neurotoxicity onset was 2 days and the median time to resolution was 5 days
  - HLH/MAS (potential complications related to excessive immune activation associated with CAR T cell therapies) occurred in 4% of patients, including two patients: one who developed fatal multiorgan HLH/MAS with CRS and the second patient with fatal bronchopulmonary aspergillosis with HLH/MAS as a contributing factor

Post-Marketing Requirement (PMR) study
A PMR study has been required to further evaluate long-term safety of ide-cel.

A post-marketing, prospective, multi-center, observational study to assess the long-term safety of ide-cel and the risk of secondary malignancies occurring after treatment with ide-cel. The study will include at least 1500 adult patients with R/R MM after four or more prior lines of systemic therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody; the enrolled patients will be followed for 15 years after product administration.

A digital platform, Cell Therapy 360, is provided by the manufacturer (BMS) to support the patient and physician treatment experience. Patients will be able to track production and receive support and other relevant information. The manufacturer will also provide patients with wearable technology to help patients track their temperature in real time.

Ongoing Clinical Trials
Abecma is being evaluated in several clinical trials in the U.S.

Phase 3 trial includes:
- Abecma vs standard treatment regimens for patients with R/R MM (KarMMa-3 trial; NCT03651128)

Phase 1 and 2 trials include:
- Abecma in patients with R/R MM and in patients with high-risk MM (KarMMa-2 trial; NCT03601078)
Abecma (idecabtagene vicleucel; ide-cel)

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- Abecma in patients with high-risk, newly diagnosed MM (KarMMa-4 trial; NCT04196491)

Comparative Studies

A head-to-head trial and indirect treatment comparison studies evaluating the safety and efficacy of FDA-approved CAR T-cell therapies for R/R MM patients are lacking. Furthermore, there is insufficient data to perform quantitative indirect comparisons (ICER, Evidence Report April 2021).

Roex G et al. (2020) conducted a systematic review and meta-analysis assess the safety and clinical efficacy of BCMA-targeted CAR-T-cell therapies in patients with MM. The assessment included 27 clinical studies pertaining to 23 different BCMA CAR-T-cell therapies in 640 patients. It is noted that high response rates were achieved for all BCMA CAR-T patients evaluable for clinical response and along with high response rates, toxicity was also high (80.3% patients evaluable for safety experienced CRS with 14.1% experiencing CRS of grade ≥3) with high dose ide-cel and cilta-cel having higher than average rates of CRS overall (96.3% and 89.5%, respectively).

- The response rates for high dose ide-cel and cilta-cel were comparable (ORR 82% and 88%, respectively).
- The median PFS among evaluable patients treated with high-dose ide-cel was 12.1 months and 19.9 months for patients treated with cilta-cel.

This meta-analysis provides evidence that despite toxicities, BCMA CAR-T therapies are considered highly efficacious, even in heavily pretreated MM patients. This meta-analysis provides robust evidence for the high clinical activity of BCMA CAR-T-cell therapies in MM and shows that several patient- and treatment-related factors might contribute to their toxicity and efficacy.

National and Specialty Organizations

National Comprehensive Cancer Network (NCCN) Guidelines for Multiple Myeloma V.6.2021

Based on the review of the data and FDA approval, ide-cel is included as an option for the treatment of adult patients with R/R MM with a footnote stating, “indicated after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody” for this indication.” This is designated as a category 2A, ‘other recommended regimen.’

National Institute for Health and Care Excellence (NICE) is developing guidance on ide-cel for the treatment of patients with RRMM who have received at least 3 prior therapies [GID-TA10672]; The expected publication date is to be confirmed.


ICER has released an evidence report assessing the comparative clinical effectiveness and value of three new treatments targeting the BCMA for heavily pre-treated patients with triple class refractory MM who have cycled through numerous previous lines of therapy: Abecma (ide-cel), cilta-cabtagene autoleucel (‘cilta-cel’) and Blenrep (belantamab).

A systematic review of cilta-cel and Abecma suggests that the evidence is insufficient to determine whether one agent is superior to the other. It was concluded that ‘belantamab is promising but inconclusive compared to usual care for patients with triple-, quad- and penta- refractory MM exposed to 4+ prior lines of treatment. The overall response rate and overall survival suggests a possible small net benefit. However, the frequency and severity of visual impairment and lack of demonstrated improvement in health-related quality of life suggests that any net benefits are likely to be modest. The current evidence precludes a substantial benefit; additional data is required to preclude small overall net harm.’ The key findings summarized by the report are as follows:

- While the data are limited and toxicities are common, both Abecma and cilta-cel appear to deliver relatively sizeable gains in both progression-free survival and overall survival for triple class refractory MM patients exposed to three or more prior lines of treatment, with higher rates of response and longer survival than treatment with current therapies. Based on this evidence, ICER determined that there is high certainty that both therapies provide at least a small net health benefit compared to usual care, with the possibility of a substantial benefit (“B+”). The evidence remains insufficient (“I”) to compare ide-cel and cilta-cel to each other.

- Belantamab appears to be equivalent or slightly superior to current treatments for triple class refractory MM patients exposed to four or more prior lines of treatment. However, visual disturbances and other toxicities are also common with belantamab, requiring dose reduction or discontinuation in some circumstances. ICER rated the current evidence promising but inconclusive (“P/I”), as the balance of potential benefits and risks did not rule
American Society of Clinical Oncology (ASCO) issued a CAR T-Therapy Policy Brief in 2019 supporting coverage of CAR T-cell therapy for all FDA-approved indications.

### Chimeric Antigen Receptor T-cells (CAR T-cells)

CAR T-cells are most often used to treat hematological malignancies, and a common target is B-cell cluster of differentiation antigen 19 (CD19). CAR T-cell infusion is typically administered in an outpatient setting, although patients receiving treatment may require an inpatient stay if adverse events are encountered. Patients typically must remain close to the treatment facility or clinic for a period of up to 6-8 weeks for monitoring and rapid identification of treatment-related adverse events that require hospitalization. CAR T therapy is associated with serious complications, including some fatal neurologic events and CRS, which is a severe systemic response (e.g., high fever, flu-like symptoms, hypotension, mental status changes) to the activation and proliferation of CAR T-cells. CRS is observed in nearly all treated patients and may be life-threatening, but it typically responds to treatment with aggressive supportive care that includes tocilizumab and corticosteroids. Neurologic toxicities may also be severe or life-threatening. Other adverse events include hypersensitivity reactions, serious infections, prolonged cytopenias, prolonged hypogammaglobulinemia, and second malignancies.

### Cytokine release syndrome (CRS)

An acute systemic inflammatory response syndrome characterized by fever, with or without multiple organ dysfunction that is associated with CAR-T cell therapy or other forms of immunotherapy. Clinical manifestations include fever, which may be accompanied by fatigue, headache, rash, diarrhea, arthralgia, and myalgia. Milder CRS can progress to a more severe syndrome, which may include hypotension, hypoxia, and uncontrolled systemic inflammatory response with circulatory collapse, vascular leakage, peripheral and/or pulmonary edema, renal failure, cardiac dysfunction, and multiorgan system failure.

### Eastern Cooperative Oncology Group Performance Status (ECOG PS)

A scale used to determine the individual's level of functioning; standard criteria for measuring how the disease impacts a patient's daily living abilities:

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>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</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Deceased</td>
</tr>
</tbody>
</table>

The scale was developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group and published in 1982.

### Coding & Billing Information

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
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<tr>
<td>0537T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day</td>
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<td>0538T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)</td>
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<tr>
<td>0539T</td>
<td>Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for</td>
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Abecma (idecabtagene vicleucel; ide-cel)

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administration

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<th>HCPCS</th>
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<td>C9399</td>
<td>Unclassified drugs or biologicals (hospital outpatient use only) [Abecma]</td>
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<td>J3490</td>
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<tr>
<td>J9999</td>
<td>Not otherwise classified, antineoplastic drugs</td>
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</table>

AVAILABLE DOSAGE FORMS: 50mL, 250mL, and 500mL infusion bags containing a frozen suspension of genetically modified autologous T cells in 5% DMSO. A single dose of contains a cell suspension of 300 to 460 x 106 CAR-positive T cells in 1 or more infusion bags.

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/9/2021 MCPC New policy. IRO Peer Review. 4/21/2021. Policy was reviewed by practicing physician Board-certified in Hematology & Oncology.
Policy converted to new template in Sep 2021.

REFERENCES

Government Agency


• NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). Available at: CMS NCD
• Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N). Available at: CMS

ClinicalTrials.gov.

• ClinicalTrials.gov Identifier: NCT03651128. Efficacy and safety study of bb2121 in subjects with relapsed and refractory multiple myeloma (KarMMa). Available at: https://clinicaltrials.gov/ct2/show/NCT03651128 Accessed April 2021

U.S. Food and Drug Administration (FDA)

• U.S. FDA Approves Bristol Myers Squibb’s and bluebird bio’s Abecma (idecabtagene vicleucel), the First Anti-BCMA CAR T Cell Therapy for Relapsed or Refractory Multiple Myeloma. FDA. Published March 26, 2021. Accessed April 2021. Available at: Link

Prescribing Information and Drug Compendia

Abecma (idecabtagene vicleucel) [Prescribing Information]. Summit, NJ: Celgene Corporation; March 2021.


Peer Reviewed Publications


National and Specialty Organizations


American Cancer Society. Key Statistics About Multiple Myeloma. Available at ACS. January 12, 2021; Accessed: April 2021


National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Program. Cancer Stat Facts: Myeloma. Available at SEER or Accessed April 2021


Other Peer Reviewed and Professional Organization Publications (used in the development of this policy)


• Multiple myeloma: Regimens used for relapsed or refractory disease. Topic 121127 Version 34.0. Topic last updated: Mar 30, 2021
• Multiple myeloma: Treatment of relapsed or refractory disease. Topic 6661 Version 119.0. Topic last updated: Mar 30, 2021
• Cytokine release syndrome (CRS). Topic 118012 Version 6.0. Topic last updated Dec 18, 2020
Reserved for State specific information (to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.

Centers for Medicare & Medicaid Services (CMS)
On August 7th, 2019 CMS published a National Coverage Determination (NCD) regarding CAR-T therapy coverage in the Medicare program. According to the NCD, for services performed on or after August 7, 2019, CMS covers autologous treatment for cancer with T-cells expressing at least one chimeric antigen receptor (CAR) when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies (REMS) and used for a medically accepted indication as defined at Social Security Act section 1861(t)(2) -i.e., is used for either an FDA-approved indication (according to the FDA-approved label for that product), or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia. Reference Publication 100-03, National Coverage Determination (NCD) Manual Section 110.24 for complete coverage criteria. (Rev. 10454, Issued: 11-13-20, Effective: 08-07-19, Implementation: 02-16-21)

NOTE: On 11/2020, a Change Request (CR) was issued to inform of coverage effective for claims with dates of service on or after August 7, 2019 [Link: TN 10454 (Medicare Claims Processing)]