Idecabtagene vicleucel (ide-cel, bb2121, Abecma; Bristol Myers Squibb)
FDA Approval Date: 3/26/2021

AHFS PHARMACOLOGIC THERAPEUTIC CLASS¹
26:12 - Gene Therapy; 10:00 - Antineoplastic Agents

LEXI-COMP PHARMACOLOGIC THERAPEUTIC CLASS²
Antineoplastic agent, Anti-BCMA; Antineoplastic agent, CAR-T Cell Immunotherapy; Cellular Immunotherapy, Autologous; Chimeric Antigen Receptor T-Cell Immunotherapy

NCCN CATEGORY¹
Category 2A

CURRENT FORMULARY STATUS WITHIN ENTERPRISE
Non-formulary

AVAILABLE FORMULATIONS³
Suspension, intravenous: 50 mL, 250 mL, 500 mL

INDICATIONS²
FDA Approved
Multiple myeloma, relapsed or refractory (RRMM) - in adults after >4 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
Off-Label uses
None

DESCRIPTION AND CLINICAL PHARMACOLOGY¹²
Idec-cel is a B-cell maturation antigen (BMCA)-directed, genetically modified, autologous T-cell immunotherapy in which a patient's T-cells are harvested through leukapheresis and then genetically modified via transduction ex vivo with an anti-BCMA02 chimeric antigen receptor (CAR) lentiviral vector (LVV). Antigen-specific activation of Idec-cel results in CAR-positive T-cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells once injected back into the patient.

Abecma is the first approved CAR-T cell therapy that targets the BCMA protein. There are four other CAR-T treatments available in the U.S. that are produced the same way, but they are engineered to target a protein called CD19 instead.

PHARMACODYNAMICS AND PHARMACOKINETICS²³⁴

<table>
<thead>
<tr>
<th>Onset</th>
<th>Rapid decreases in tumor markers associated with clinical response, including serum levels of soluble BCMA, and bone marrow CD138+ cells, as well as MRD negative responses, were observed within the first month.</th>
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<tbody>
<tr>
<td>Time to Peak</td>
<td>Peak levels of plasma cytokines, chemokines, and soluble immune mediators were observed within 14 days of infusion; these levels typically returned to baseline within 1 month.</td>
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<tr>
<td>Duration of Action</td>
<td>Ide-cel can persist in peripheral blood for up to 1 year after infusion.</td>
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<tr>
<td>Expansion</td>
<td>Ide-cel exhibits an initial rapid expansion followed by a bi-exponential decline. Patients who receive tocilizumab and/or corticosteroids to manage cytokine release syndrome (CRS) and/or neurologic toxicity experienced higher Ide-cel expansion levels and higher AUC₀⁻₂₈ and Cₘₐₓ compared to patients who did not. The median time to maximal expansion in peripheral blood (Tmax) occurred 11 days.</td>
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</tbody>
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DOsing and Administration²³

Adult
- For autologous IV use only. Confirm patient identity matches cassette and infusion bag prior to infusion.
- A treatment course of lymphodepleting chemotherapy, with fludarabine and cyclophosphamide, for 3 days, followed by Ide-cel infusion 2 days after completion.
- Delay Ide-cel infusion up to 7 days for unresolved serious adverse events (pulmonary or cardiac events, or hypotension), including events due to prior chemotherapies, and for active infections or inflammatory disorders.
- Ensure tocilizumab (at least 2 doses) and emergency equipment are available prior to infusion and during recovery period.
- Premedication - Premedicate with acetaminophen 650 mg orally and diphenhydramine 12.5 mg IV or 25-50mg orally ~30-60 minutes prior to Ide-cel infusion. Avoid prophylactic dexamethasone or other systemic corticosteroids as they may interfere with Ide-cel activity. Administer prophylactic antimicrobials as clinically indicated. Consider antiviral therapy to prevent viral reactivation as appropriate.
- Administer at a REMS-certified healthcare facility.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing</th>
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<tbody>
<tr>
<td>Multiple myeloma, released or refractory - IV</td>
<td>Target dose: 300 to 460 x 10^6 CAR-positive viable T-cells. Provided as a single dose for infusion containing a suspension of CAR-positive T cells in one or more infusion bags (average: 3 infusion bags per patient)</td>
</tr>
</tbody>
</table>

Geriatric
- Refer to adult dosing

Pediatric
- The safety and efficacy in patients under 18 years of age has not been studied.

Renal impairment
- Has not been studied - there are no dosage adjustments provided in the manufacturer’s labeling

Hepatic impairment
- Has not been studied - there are no dosage adjustments provided in the manufacturer’s labeling

LITERATURE REVIEW AND CLINICAL EFFICACY¹
In the Phase 2 KarMMA clinical study, Abecma demonstrated an overall response rate (ORR) of 72%, stringent complete response rate (sCR) of 28%, median progression-free survival (PFS) of 8.8 months overall, a PFS of 20.2 months among patients with a complete response (CR) or better, and a median overall survival (OS) of 19.4 months.

CONTRAINdications, WARNings, AND PRECAUTIONS¹²³

Black Box Warnings
- Cytokine Release Syndrome (CRS)
  - Any-grade CRS was observed in 84% of patients, grade 3-4 occurred in 5%
  - Median time to onset 1 day, median duration 5 days
  - Tocilizumab use 52%, glucocorticoid use 15%
- Neurologic Toxicities
  - Any-grade neurotoxicity occurred in 18% of patients, grade 3 occurred in 3% of patients
  - Median time to onset 2 days, median duration 3 days
- Hemophagocytic lymphohistiocytosis/macrophage activation syndrome
  - HLH/MAS occurred in 4% of patients
Median time to onset of 7 days
- Prolonged cytopenia
  - Prolonged grade 3 or 4 neutropenia occurred in 41% of patients, grade 3 or 4 thrombocytopenia occurred in 49% of patients
- REMS program

Contraindications
There are no contraindications listed in the manufacturer’s labeling.

Warnings and Precautions
- Cytomegalovirus reactivation
  - Infection resulting in pneumonia and death has occurred
- Hepatitis B virus reactivation
  - Reactivation (sometimes resulting in fulminant hepatitis, hepatic failure, and death) can occur in patients treated with medication directed against plasma cells
- Hypersensitivity
  - Ide-cel contains dimethyl sulfoxide (DMSO), which has been associated with serious hypersensitivity reactions, including anaphylaxis.
- Hypogammaglobulinemia and plasma cell aplasia
- Infections
  - Severe, life-threatening, or fatal infections have occurred. Infections include bacterial, viral, and fungal as well as unspecified pathogens.
- Secondary malignancies

ADVERSE REACTIONS

Common
- Cardiovascular - Edema (25%)
- Gastrointestinal - Decrease in appetite (22%), Diarrhea (35%), Nausea (29%)
- Musculoskeletal - Musculoskeletal pain (45%)
- Neurologic - Headache (23%)
- Respiratory - Cough (23%), Upper respiratory infection (34%)
- Other - Fatigue (45%), Fever (25%)  

Serious
- See “Contraindications, Warnings, and Precautions” above
- Other
  - Neurologic - Aphasia (7%), Cerebral Edema, Encephalopathy (26%), Parkinsonism, Tremor (10%)
  - Psychiatric - Delirium (6%)

Dose Adjustments for Toxicity
Cytokine Release Syndrome

<table>
<thead>
<tr>
<th>CRS Grade</th>
<th>Tocilizumab</th>
<th>Corticosteroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1: symptomatic treatment only</td>
<td>If ≥72h after infusion, manage symptomatically. If &lt;72h, consider tocilizumab 8mg/kg IV over 1h</td>
<td>Consider dexamethasone 10 mg IV every 24h</td>
</tr>
<tr>
<td>Grade 2: symptoms require and respond to moderate intervention</td>
<td>Administer tocilizumab 8mg/kg IV over 1h. Repeat every 8h PRN if not responsive to IV fluids or increasing supp. Oxygen. Max of 3</td>
<td>Consider dexamethasone 10 mg IV every 12-24h</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>Corticosteroids and Anti Seizure medication</td>
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<td>--------------</td>
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</tbody>
</table>
| Grade 1: | Initiate seizure prophylaxis with non sedating anti seizure medications (i.e Keppra).
If >72h after infusion, observe the patient. If <72h, consider dexamethasone 10 mg IV every 12-24h for 2-3 days. |
| Grade 2: | Initiate seizure prophylaxis with non sedating anti seizure medications (i.e Keppra).
Initiate dexamethasone 10 mg IV every 12h for 2-3 days (or longer if persistent). Consider taper for a total corticosteroid exposure >3 days. They are not recommended for isolated grade 2 headaches.
If no improvement after 24h or worsening of neurologic toxicity, increase dexamethasone dose and/or frequency up to a max of 20 mg IV every 6h. |
| Grade 3: | Initiate seizure prophylaxis with non sedating anti seizure medications (i.e Keppra).
If no improvement after 24h or worsening of neurologic toxicity, escalate to methylprednisolone (2mg/kg IV loading dose, followed by 0.5mg/kg IV every 6h, taper within 7 days
If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Administer methylprednisolone 1-2g IV, repeat every 24h if needed and taper as clinically indicated. Administer cyclophosphamide 1.5g/m^2 IV. |
| Grade 4: | Initiate seizure prophylaxis with non sedating anti seizure medications (i.e Keppra).
Initiate dexamethasone 20 mg IV every 6h.
If no improvement after 24h or worsening of neurologic toxicity, administer methylprednisolone 1-2g IV, repeat every 24h if needed and taper as clinically indicated.
If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Administer methylprednisolone 1-2g IV, repeat every 24h if needed and taper as clinically indicated. Administer cyclophosphamide 1.5g/m^2 IV. |
### Toxicity Management

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Management</th>
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</thead>
<tbody>
<tr>
<td>Cytomegalovirus reactivation</td>
<td>Manage as clinically appropriate</td>
</tr>
<tr>
<td>Cytopenias</td>
<td>Manage cytopenia with myeloid growth factor and blood product transfusion support</td>
</tr>
<tr>
<td>Hypogammaglobulinemia (IgG &lt;400 mg/dL)</td>
<td>Administer IV immune globulin and manage as indicated with infection precautions and antibiotic and/or antiviral prophylaxis</td>
</tr>
<tr>
<td>Infection</td>
<td>Administer prophylactic, preemptive, and/or therapeutic antimicrobials according to standard institutional guidelines</td>
</tr>
<tr>
<td>Neutropenic fever</td>
<td>Evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as clinically indicated</td>
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</tbody>
</table>

### RISK EVALUATION AND MITIGATION STRATEGIES³

**ABECMA REMS**
- Healthcare facilities that dispense and administer Ide-cel must be enrolled and comply with the REMS requirements
- Certified healthcare facilities must have one-site, immediate access to tocilizumab (at least 2 doses) for each patient for infusion within 2 hours, if needed for treatment of CRS
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer ide-cel are trained in the management of CRS and neurologic toxicities
- Further information is available at [www.AbecmaREMS.com](http://www.AbecmaREMS.com) or contact Bristol-Myers Squibb at 1-888-423-5436

### MAJOR INTERACTIONS²³

**Drug-Drug (Risk X - Avoid Combination)**
- **Immunizations**
  - Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during Ide-cel treatment, and until immune recovery following treatment with Ide-cel. Immunization with live viral vaccines during or following Ide-cel has not been studied.
  - Measles, Mumps, and Rubella Virus Vaccine - immunosuppressants may enhance the adverse/toxic effects of MMR Virus Vaccine
  - Varicella Virus Vaccine - immunosuppressants may enhance the adverse/toxic effect of Varicella Virus Vaccine
- **BCG (Intravesical) - immunosuppressants may diminish the therapeutic effect of BCG**
- **Cladribine - may enhance the immunosuppressive effect of immunosuppressants**
- **Corticosteroids - avoid use of prophylactic corticosteroids**
- **Natalizumab - immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased**
- **Pimecrolimus - the adverse/toxic effects of immunosuppressants**
- **Tacrolimus (topical) - may enhance the adverse/toxic effects of immunosuppressants**
- **Talimogene Laherparepvec - immunosuppressants may enhance the adverse/toxic effects of talimogene laherparepvec. Specifically, the risk for disseminated herpetic infection may be increased**
- **Upadacitinib - immunosuppressants may enhance the immunosuppressive effect of upadacitinib**
**Drug-Disease**
- HIV and the lentivirus used to make ide-cel have limited, short spans of identical genetic material (RNA). Therefore, some commercial HIV nucleic acid tests may yield false-positive results in patients who have received Ide-cel.

**MONITORING REQUIREMENTS**
- Screen for HBV, HCV, and HIV prior to collection of cells for manufacturing.
- Monitor CBC prior to and after administration.
- Evaluate pregnancy status prior to use.
- Monitor immunoglobulin levels (IgG) after treatment.
- Monitor patients daily (for signs/symptoms of cytokine release syndrome and neurotoxicity) at the health care facility for at least 7 days after cell infusion. Patient should remain within proximity of the facility for at least 4 weeks after infusion.
- Monitor for signs/symptoms of cytomegalovirus and HBV reactivation, hypersensitivity, HLH/MAS, and secondary malignancies.

**PREGNANCY/BREASTFEEDING**
- Verify pregnancy status prior to treatment initiation.
- There is no evidence regarding Ide-cel safety in pregnancy. Animal studies have not been conducted. Based on the mechanism of action, if the transduced cells cross the placenta, they may cause fetal toxicity, including plasma cell aplasia or hypogammaglobulinemia. Therefore, it is not recommended to use in women who are pregnant.
- It is not known if Ide-cel is present in breast milk. Considerations for risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother are recommended prior to making the decision to breastfeed.

**MEDICATION SAFETY ISSUES**

**Sound/Look Alike issues**
- Ide-cel may be confused with axicabtagene ciloleucel, brexucabtagene autoleucel, lisocabtagene maraleucel, sipuleucel-T, tisagenlecleucel.
- Ciltacabtagene autoleucel, a pipeline CAR-T product by Johnson & Johnson could eventually be a competitor of Abecma.

**High Alert Medication**
- This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its lists of drug classes which have heightened risk for causing significant patient harm when used in error.

**SPECIAL STORAGE PRECAUTIONS**
- Store frozen in the vapor phase of liquid nitrogen. Product is shipped in the vapor phase of a liquid nitrogen shipper. If the infusion site is qualified for onsite storage, transfer Ide-cel to the onsite vapor phase of liquid nitrogen storage prior to preparation. If they are not qualified, contact the manufacturer to arrange for return shipment if the patient is not receiving infusion same-day.
- Ide-cel is stable for 2 hours at room temperature once thawed; administer within 1 hour of the start to thaw.

**SPECIAL HANDLING/ADMINISTRATION**
- Before thawing, inspect the infusion bag(s) for breaches of container integrity (i.e breaks or cracks); contact the manufacturer if compromised. If >1 bag is received, thaw 1 bag at a time and do not initiate thawing of the next bag until infusion of the previous bag is complete.
To thaw, place the bag inside a second sterile bag and thaw at ~37°C using an appropriate thaw device or water bath) until there is no visible ice in the infusion bag.

- Gently mix the bag contents to disperse cellular material clumps. If visible clumps remain, continue to gently mix the contents.
- Do not wash, spin down, and/or resuspend in new media prior to infusion.
- Prime tubing set with NS prior to infusion. Infuse Ide-cel by gravity infusion within 1 hour after the start of thaw. After the entire contents have been infused, rinse tubing with 30-60mL NS to ensure all product was delivered.
- Do not use a leukodepletion filter. A central line may be used for administration.

### COST AND REIMBURSEMENT INFORMATION¹

<table>
<thead>
<tr>
<th>Cost (Estimated)</th>
<th>$419,500</th>
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<tbody>
<tr>
<td><strong>Sales Projections (Estimated)</strong></td>
<td>Analysts are predicting sales to be $103 million in 2021, $328 million in 2022, growing to $1.1 billion in 2025.</td>
</tr>
<tr>
<td><strong>Medical/Pharmacy Benefit</strong></td>
<td>Medical</td>
</tr>
<tr>
<td><strong>Inpatient/Outpatient</strong></td>
<td>Inpatient and outpatient</td>
</tr>
</tbody>
</table>
| **Reimbursement Code** | 50 mL infusion bag and metal cassette [NDC 59572-0515-01]  
250 mL infusion bag and metal cassette [NDC 59572-0515-02]  
500 mL infusion bag and metal cassette [NDC 59572-0515-03] |
| **NOC Code Billing Guide** | C9399 Unclassified drugs or biologicals (hospital outpatient use)  
J9999 not otherwise classified, antineoplastic drugs |

### REFERENCES