ABECMA® (idecabtagene vicleucel), suspension for intravenous infusion

Initial U.S. Approval: 2021

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA, AND SECONDARY HEMATOLOGICAL MALIGNANCIES

See full prescribing information for complete boxed warning.

• Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids (2.2, 2.3, 5.1).
• Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ABECMA. Provide supportive care and/or corticosteroids as needed (2.2, 2.3, 5.3).
• Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or neurologic toxicities (5.4).
• Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA (5.8).
• T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA (5.10).
• ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS (5.5).

RECENT MAJOR CHANGES

Boxed Warning 4/2024
Indications and Usage (1) 4/2024
Dosage and Administration (2.1, 2.2) 4/2024
Warnings and Precautions (5) 4/2024

ABECMA REMS

ABECMA is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody (1).

DOSAGE AND ADMINISTRATION

For autologous use only. For intravenous use only.

• Do NOT use a leukodepleting filter (2.2).
• Administer a lymphodepleting chemotherapy regimen of cyclophosphamide and fludarabine before infusion of ABECMA (2.2).
• Confirm the patient's identity prior to infusion (2.2).
• Premedicate with acetaminophen and an H1-antihistamine (2.2).
• Avoid prophylactic use of dexamethasone or other systemic corticosteroids (2.2).
• Confirm availability of tocilizumab prior to infusion (2.2, 5.2).
• Dosing of ABECMA (idecabtagene vicleucel) is based on the number of chimeric antigen receptor (CAR)-positive T cells (2.1).
• The recommended dose range is 300 to 510 x 10^6 CAR-positive T cells (2.1).
• Administer ABECMA at a certified healthcare facility (2.2, 5.2, 5.3, 5.4).

CONTRAINDICATIONS

None (4).

WARNINGS AND PRECAUTIONS

• Hypersensitivity Reactions: Monitor for hypersensitivity reactions during infusion (5.6).
• Infections: Monitor patients for signs and symptoms of infection; treat appropriately (5.7).
• Prolonged Cytopenias: Patients may exhibit prolonged Grade 3 or higher cytopenias following ABECMA infusion. Monitor blood counts prior to and after ABECMA infusion (5.8).
• Hypogammaglobulinemia: Monitor and consider immunoglobulin replacement therapy (5.9).
• Secondary Malignancies: T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. In the event that a secondary malignancy occurs after treatment with ABECMA, contact Bristol-Myers Squibb at 1-888-905-4055 (5.10).
• Effects on Ability to Drive and Use Machines: Advise patients to refrain from driving or operating heavy or potentially dangerous machines for at least 8 weeks after ABECMA administration (5.11).

ADVERSE REACTIONS

The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) include pyrexia, CRS, hypogammaglobulinemia, infections – pathogen unspecified, musculoskeletal pain, fatigue, febrile neutropenia, hypotension, tachycardia, diarrhea, nausea, headache, chills, upper respiratory tract infection, encephalopathy, edema, dyspnea and viral infections (6.1).

The most common Grade 3 or 4 laboratory adverse reactions (incidence greater than or equal to 50%) include leukocyte count decreased, neutrophil count decreased, lymphocyte count decreased, platelet count decreased, and hemoglobin decreased (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.
ABECMA® (idecabtagene vicleucel)

FULL PRESCRIBING INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAST, PROLONGED CYTOPENIA, AND SECONDARY HEMATOLOGIC MALIGNANCIES

- Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids [see Dosage and Administration (2.2, 2.3), Warnings and Precautions (5.2), and Adverse Reactions (6.1)].
- Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ABECMA. Provide supportive care and/or corticosteroids as needed [see Dosage and Administration (2.2, 2.3) and Warnings and Precautions (5.3)].
- Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAST) including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAST can occur with CRS or neurologic toxicities [see Warnings and Precautions (5.4)].
- Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA [see Warnings and Precautions (5.8)].
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA [see Warnings and Precautions (5.10)].
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS [see Warnings and Precautions (5.5)].

1 INDICATIONS AND USAGE

ABECMA is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

2 DOSAGE AND ADMINISTRATION

For autologous use only. For intravenous use only.

2.1 Dose

ABECMA is provided as a single dose for infusion containing a suspension of chimeric antigen receptor (CAR)-positive T cells in one or more infusion bags. The recommended dose range is 300 to 510 x 10^6 CAR-positive T cells.

See the accompanying Release for Infusion Certificate (RFI Certificate) for additional information pertaining to dose [see How Supplied/Storage and Handling (16)].

2.2 Administration

ABECMA is for autologous use only. The patient's identity must match the patient identifiers on the ABECMA cassette(s) and infusion bag(s). Do not infuse ABECMA if the information on the patient-specific label(s) does not match the intended patient.

Preparing Patient for ABECMA Infusion

Confirm the availability of ABECMA prior to starting the lymphodepleting chemotherapy regimen.

Pretreatment

Administer the lymphodepleting chemotherapy regimen: cyclophosphamide 300 mg/m^2 intravenously (IV) and fludarabine 30 mg/m^2 IV for 3 days.

See the prescribing information of cyclophosphamide and fludarabine for information on dose adjustment in renal impairment.

Administer ABECMA 2 days after completion of lymphodepleting chemotherapy.

Delay the infusion of ABECMA up to 7 days if a patient has any of the following conditions:
- unresolved serious adverse events (especially pulmonary events, cardiac events, or hypotension), including those after preceding chemotherapies.
- active infections or inflammatory disorders [see Warnings and Precautions (5.7)].

Premedication

Administer acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally, or another H1-antihistamine) approximately 30 to 60 minutes before infusion of ABECMA.

Avoid prophylactic use of dexamethasone or other systemic corticosteroids, as the use may interfere with the activity of ABECMA.

ABECMA® (idecabtagene vicleucel)

Receipt of ABECMA

- ABECMA is shipped directly to the cell laboratory or clinical pharmacy associated with the infusion center in the vapor phase of a liquid nitrogen shipper.
- Confirm the patient's identity with the patient identifiers on the shipper.
- If the patient is not expected to be ready for same-day administration before the shipper expires and the infusion site is qualified for onsite storage, transfer ABECMA to onsite vapor phase of liquid nitrogen storage.
- If the patient is not expected to be ready for same day administration before the shipper expires and the infusion site is not qualified for onsite storage, contact Bristol-Myers Squibb at 1-888-805-4555 to arrange for return shipment.

Preparation of ABECMA for infusion

1. Coordinate the timing of ABECMA thaw and infusion. Confirm the infusion time in advance and adjust the start time of the thaw of ABECMA so that it will be available for infusion when the patient is ready.
2. Prior to thawing the product, confirm that tocilizumab and emergency equipment are available prior to the infusion and during the recovery period.
3. An ABECMA dose may be contained in one or more patient-specific infusion bags. Verify the number of bags received for the indicated dose of ABECMA prior to preparation of ABECMA for infusion.
4. Confirm patient identity: Prior to preparation of ABECMA, match the patient's identity with the patient identifiers on the ABECMA cassette(s), infusion bag(s), and the RFI Certificate.

Note: The patient identifier number may be preceded by the letters DIN or APh ID.

5. Do not remove the ABECMA infusion bag(s) from the cassette(s) if the information on the patient-specific cassette label(s) does not match the intended patient. Contact Bristol-Myers Squibb at 1-888-805-4555 if there are any discrepancies between the labels and the patient identifiers.
6. Once patient identity is confirmed, remove the ABECMA infusion bag(s) from the cassette(s) and check that the patient information on the cassette label(s) matches the patient information on the bag label(s).

Figure 1: ABECMA Bag Label(s)

7. Inspect the infusion bag(s) for any breaches of container integrity such as breaks or cracks before thawing. If the bag(s) is compromised, do not administer and contact Bristol-Myers Squibb at 1-888-805-4555.
8. If more than one infusion bag has been received to achieve the treatment dose, thaw each infusion bag one at a time. Do not initiate thaw of the next bag until infusion of the previous bag is complete.
9. Place the infusion bag(s) inside a second sterile bag per local guidelines.
10. Thaw ABECMA infusion bag(s) at approximately 37°C using an approved thaw technique. Gently mix the contents of the bag to disperse clumps of cellular material. If cell clumps remain, continue to gently mix the contents of the bag. Small clumps of cellular material should disperse with gentle manual mixing. Do not wash, spin down, and/or resuspend ABECMA in new media prior to infusion.
11. ABECMA should be administered within 1 hour of the start of thaw. ABECMA is stable for 2 hours at room temperature once thawed.

ABECMA Administration

- For autologous use only.
- Do NOT use a leukodepleting filter.
- Ensure that a minimum of 2 doses of tocilizumab and emergency equipment are available prior to infusion and during the recovery period.
- Central venous access may be utilized for the infusion of ABECMA and is encouraged in patients with poor peripheral access.

1. Confirm that the patient's identity matches the patient identifiers on the ABECMA infusion bag(s).
2. Prime the tubing of the infusion set with normal saline prior to infusion.
3. Infuse the entire contents of the ABECMA infusion bag within 1 hour after start of thaw by gravity flow.
4. After the entire content of the infusion bag is infused, rinse the tubing with 30 to 60 mL of normal saline at the same infusion rate to ensure all product is delivered.

5. If more than one infusion bag has been received, administer all bags as directed, following steps 1-4 for all subsequent infusion bags. Do not initiate thaw of the next bag until infusion of the previous bag is complete.

ABECMA contains human blood cells that are genetically modified with replication-incompetent, self-inactivating lentiviral vector. Follow universal precautions and local biosafety guidelines for handling and disposal of ABECMA to avoid potential transmission of infectious diseases.

Monitoring

- Administer ABECMA at a REMS-certified healthcare facility.
- Monitor patients at least daily for 7 days following ABECMA infusion at the certified healthcare facility for signs and symptoms of CRS and neurologic toxicities [see Warnings and Precautions (5.2, 5.3)].
- Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.
- Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following infusion.

2.3 Management of Severe Adverse Reactions

Cytokine Release Syndrome (CRS)

Identify CRS based on clinical presentation [see Warnings and Precautions (5.2)]. Evaluate for and treat other causes of fever, hypoxia, and hypotension. If CRS is suspected, manage according to the recommendations in Table 1.

Patients who experience CRS should be closely monitored for cardiac and organ function until resolution of symptoms. Consider antiseizure prophylaxis with levetiracetam in patients who experience CRS.

Patients who experience Grade 2 or higher CRS (e.g., hypotension not responsive to fluids, or hypoxia requiring supplemental oxygenation) should be monitored with continuous cardiac telemetry and pulse oximetry.

For severe or life-threatening CRS, consider intensive care unit level monitoring and supportive therapy.

For CRS refractory to first line interventions such as tocilizumab or tocilizumab and corticosteroids, consider alternate treatment options (i.e., higher corticosteroid dose, alternative anti-cytokine agents, anti-T cell therapies). Refractory CRS is characterized by fevers, end-organ toxicity (e.g., hypoxia, hypotension) not improving within 12 hours of first line interventions or development of hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS).

If concurrent neurologic toxicity is suspected during CRS, administer:

- Corticosteroids according to the more aggressive intervention based on the CRS and neurologic toxicity grades in Tables 1 and 2
- Tocilizumab according to the CRS grade in Table 1
- Antiseizure medication according to the neurologic toxicity in Table 2

<table>
<thead>
<tr>
<th>CRS Grade</th>
<th>Tocilizumab</th>
<th>Corticosteroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>If onset 72 hours or more after infusion, treat symptomatically. If onset less than 72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).</td>
<td>Consider dexamethasone 10 mg IV every 24 hours.</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</td>
<td>Consider dexamethasone 10 mg IV every 12-24 hours.</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Per Grade 2 Administer dexamethasone 10 mg IV every 12 hours. If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone (20 mg IV every 6 to 12 hours). If no improvement within 24 hours or continued rapid progression, switch to methylprednisolone 2 mg/kg followed by 2 mg/kg divided 4 times per day. After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</td>
<td></td>
</tr>
<tr>
<td>Grade 4</td>
<td>Per Grade 2 Administer dexamethasone 20 mg IV every 6 hours. After 2 doses of tocilizumab, consider alternative anti-cytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total. If no improvement within 24 hours, consider methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated) or other anti-T cell therapies.</td>
<td></td>
</tr>
</tbody>
</table>

| Neurologic Toxicity |

Monitor patients for signs and symptoms of neurologic toxicities (Table 2). Rule out other causes of neurologic signs or symptoms. Provide intensive care supportive therapy for severe or life-threatening neurologic toxicities. If neurologic toxicity is suspected, manage according to the recommendations in Table 2.

If concurrent CRS is suspected during the neurologic toxicity event, administer:

- Corticosteroids according to the more aggressive intervention based on the CRS and neurologic toxicity grades in Tables 1 and 2
- Tocilizumab according to CRS grade in Table 1
- Antiseizure medication according to neurologic toxicity in Table 2

a Lee criteria for grading CRS (Lee et al., 2014).

b If corticosteroids are initiated, continue corticosteroids for at least 3 doses, and taper over a maximum of 7 days.

c Refer to tocilizumab Prescribing Information for details.
Table 2: Neurologic Toxicity Grading and Management Guidance

<table>
<thead>
<tr>
<th>Neurologic Toxicity Grade</th>
<th>Corticosteroids and Antiseizure Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Start non-sedating, antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis.</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Start non-sedating, antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. Start dexamethasone 10 mg IV every 12 hours for 2-3 days. Consider taper for a total corticosteroid exposure of greater than 3 days. Corticosteroids are not recommended for isolated Grade 2 headaches. If no improvement after 24 hours or worsening of neurologic toxicity, increase the dose and/or frequency of dexamethasone up to a maximum of 20 mg IV every 6 hours.</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Start non-sedating, antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. Start dexamethasone 10 mg IV every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to high-dose methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m².</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Start non-sedating, antiseizure medicines (e.g., levetiracetam) for seizure prophylaxis. Start dexamethasone 40 mg IV every 6 hours. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to high-dose methylprednisolone (1-2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m².</td>
</tr>
</tbody>
</table>

*NCI CTCAE criteria for grading neurologic toxicities version 4.03.

3 DOSAGE FORMS AND STRENGTHS

ABECMA® is a cell suspension for intravenous infusion. A single dose of ABECMA contains a cell suspension of 300 to 510 x 10⁶ chimeric antigen receptor (CAR)-positive T cells in one or more infusion bags [see How Supplied/Storage and Handling (16)].

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Early Death

In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared to the standard regimens arm (15/132; 11%) [see Clinical Studies (14)]. Early deaths occurred in 8% (20/254) and 0% prior to ABECMA infusion and standard regimen administration, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively. Out of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes.

5.2 Cytokine Release Syndrome (CRS)

CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed or refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N = 349), CRS occurred in 89% (310/349), including ≥Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.6% (2/349) of patients. The median time-to-onset of CRS, any grade, was 1 day (range: 1 to 27 days), and the median duration of CRS was 5 days (range: 1 to 93 days). Treatment with tocilizumab and corticosteroids was generally effective in treating CRS. Of the 349 patients who received ABECMA in clinical trials, 226 (65%) patients received tocilizumab; 39% (135/349) received a single dose, while 26% (91/349) received more than 1 dose of tocilizumab. Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS. Almost all patients who received corticosteroids for CRS also received tocilizumab. For patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells, 76% (264/349) of patients responded to tocilizumab and 35% (25/71) received at least 1 dose of corticosteroids for treatment of CRS. For patients treated in dose range of 300 to 460 x 10⁶ CAR-positive T cells, 63% (152/241) of patients received tocilizumab and 20% (49/241) received at least 1 dose of corticosteroid for treatment of CRS.

Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated [see Dosage and Administration (2.3)].

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time [see Patient Counseling Information (17)].

5.3 Neurologic Toxicities

Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), which may be severe or life-threatening, occurred concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with ABECMA. In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, CAR T-cell associated neurotoxicity occurred in 40% (139/349), including Grade 3 in 4% (14/349) and Grade 4 in 0.6% (2/349) of patients. The median time to onset of neurotoxicity was 2 days (range: 1 to 148 days). The median duration of CAR T-cell associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. CAR T cell-associated neurotoxicity resolved in 123 of 139 (88%) patients and median time to resolution was 5 days (range: 1 to 245 days). One-hundred and thirty four out of 349 (38%) patients with neurotoxicity had CRS. The onset of neurotoxicity during CRS was observed in 93 patients, before the onset of CRS in 12 patients, and after the CRS event in 29 patients. The rate of Grade 3 or 4 CAR T cell-associated neurotoxicity was 5.6% (7/124) and 3.7% (8/234) for patients treated in dose range of 460 to 510 x 10⁶ CAR-positive T cells and 300 to 460 x 10⁶ CAR-positive T cells, respectively. The most frequent (greater than or equal to 1%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

At the safety update for KarMMa-3 study, one patient developed fatal neurotoxicity 43 days after ABECMA. In KarMMa, one patient had ongoing Grade 2 neurotoxicity at the time of death. Two patients had ongoing Grade 1 tremor at the time of data cutoff. Cerebral edema has been associated with ABECMA in a patient in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have occurred after treatment with ABECMA in another study in multiple myeloma.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of neurologic toxicities. Rule out other causes of neurologic symptoms. Monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed [see Dosage and Administration (2.3)].

Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time [see Patient Counseling Information (17)].

5.4 Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS)

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, HLH/MAS occurred in 2.9% (10/349) of patients. All events of HLH/MAS had onset within 10 days of receiving ABECMA. Treatment with tocilizumab and corticosteroids was generally effective in treating HLH/MAS. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction, and cytopenia.

In KarMMa-3, one patient had Grade 5, two patients had Grade 4 and two patients had Grade 3 HLH/MAS. The patient with Grade 5 HLH/MAS also had Grade 5 candida sepsis.
and Grade 5 CRS. In another patient who died due to stroke, the Grade 4 HLH/MAS had resolved prior to death. Two cases of Grade 3 and one case of Grade 4 HLH/MAS had resolved.

In KarMMa, one patient treated in the 300 x 10^6 CAR-positive T cells dose cohort developed fatal multi-organ HLH/MAS with CRS. In another patient with fatal bronchopulmonary aspergillosis, HLH/MAS was contributory to the fatal outcome. Three cases of Grade 2 HLH/MAS resolved.

HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated. Treatment of HLH/MAS should be administered per institutional standards.

5.5 ABECMA REMS

Because of the risk of CRS and neurologic toxicities, ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS [see Boxed Warning and Warnings and Precautions (5.2, 5.3)].

The required components of the ABECMA REMS are:

- Healthcare facilities that dispense and administer ABECMA must be enrolled and comply with the REMS requirements.
- 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.
- Further information is available at www.AbecmaREMS.com or contact Bristol-Myers Squibb at 1-866-340-7332.

5.6 Hypersensitivity Reactions

Allergic reactions may occur with the infusion of ABECMA. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) in ABECMA.

5.7 Infections

ABECMA should not be administered to patients with active infections or inflammatory conditions. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion.

In all patients receiving ABECMA in the KarMMa and KarMMa-3, infections (all grades) occurred in 61% of patients. Grade 3 or 4 infections occurred in 21% of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12% of viral infections, in 7% of bacterial infections in 4.3%, and fungal infections in 1.4% of patients. Overall, 15 patients had Grade 5 infections (4.3%); 8 patients (2.3%) with infections of pathogen unspecified, 3 patients (0.9%) with fungal infections, 3 patients (0.9%) with viral infections, and 1 patient (0.3%) with bacterial infection.

Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

Febrile neutropenia was observed in 38% (133/349) of patients after ABECMA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

Viral Reactivation

Cytomegalovirus (CMV) infection resulting in pneumonia and death has occurred following ABECMA administration. Monitor and treat for CMV reactivation in accordance with clinical guidelines.

Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against plasma cells.

Perform screening for CMV, HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines before collection of cells for manufacturing.

Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

5.8 Prolonged Cytopenias

Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and ABECMA infusion.

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, 40% of patients (139/349) experienced prolonged Grade 3 or 4 neutropenia and 42% (145/349) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 59% (123/193) 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. In 76% (110/145) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 1.9 months. Five patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. The rate of Grade 3 or 4 thrombocytopenia was 62% (44/71) and 56% (135/241) for patients treated in dose range of 460 to 510 x 10^6 CAR-positive T cells and 300 to 460 x 10^6 CAR-positive T cells, respectively.
ABECMA® (idecabtagene vicleucel)

ABECMA across a dose range of 175 to 529 × 10^6 CAR-positive T cells (median dose: 445 × 10^6 CAR-positive T cells) [see Clinical Studies (14)]. Patients with a history of CNS disease or requiring ongoing treatment with chronic immunosuppression were excluded. The median age of the safety population was 63 years (range: 30 to 81 years); 43% were 65 years or older, and 63% were men. The Eastern Cooperative Oncology Group (ECOG) performance status at baseline was 0 in 47%, 1 in 51%, 2 in 1.4% and 3 in 0.5% of patients. Four (1.8%) patients treated with ABECMA had creatinine clearance <45 mL/min. For details about the study population, see Clinical Studies (14).

The most common (greater than or equal to 10%) Grade 3 or 4 nonlaboratory adverse reactions was febrile neutropenia (51%) and any infections (16%).

The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) included CRS, pyrexia, any infection, febrile neutropenia, hypogammaglobulinemia, musculoskeletal pain, hypotension, infections – pathogen unspecified, fatigue, tachycardia, diarrhea, nausea, headache, encephalopathy, dyspnea and edema.

Serious adverse reactions occurred in 43% of patients. The most common nonlaboratory (greater than or equal to 5%) serious adverse reactions included infections – pathogen unspecified (10%), pneumonia (9%), viral infections (8%), encephalopathy (6%), pyrexia (6%) and sepsis (5%). Fatal adverse reactions occurred in 9%.

Table 3 summarizes the adverse reactions that occurred in at least 10% of patients treated with ABECMA. Table 4 describes the most common Grade 3 or 4 laboratory abnormalities.

### Table 3: Adverse Reactions Observed in at Least 10% of Patients Treated in the KarMMa-3 Study

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Events</th>
<th>Grade 3 or 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>51</td>
<td>28</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>14</td>
<td>4.8</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>Nausea</td>
<td>27</td>
<td>48</td>
</tr>
<tr>
<td>Constipation</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>91</td>
<td>53</td>
</tr>
<tr>
<td>Fatigue</td>
<td>33</td>
<td>48</td>
</tr>
<tr>
<td>Edema</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>Chills</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia release syndrome</td>
<td>91</td>
<td>40</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any infection</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Infections – Pathogen unspecified</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Infections – Viral</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Infections – Bacterial</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>

Other clinically important adverse reactions that occurred in less than 10% of patients treated with ABECMA include the following:

- Cardiac disorders: cardiac arrhythmia (7%)
- Gastrointestinal disorders: gastrointestinal hemorrhage (0.5%)
- Immune system disorders: hemophagocytic lymphohistiocytosis (2.3%)
- Infections and infestations: infections – fungal (5%), sepsis (6%)
- Musculoskeletal and connective tissue disorders: motor dysfunction (9%)
ABECMA® (idecabtagene vicleucel)

- Nervous system disorders: tremor 4 (4.1%), aphasia 3 (3.2%), ataxia 3 (2.3%), seizure 0.5%
- Psychiatric disorders: anxiety 4.1%, delirium 3 (7%)
- Respiratory, thoracic, and mediastinal disorders: pulmonary edema 3 (1.4%)
- Vascular disorders: thrombosis 3 (2.3%)

- Sepsis includes bacteremia, bacterial sepsis, candida sepsis, citrobacter bacteremia, clostridial sepsis, device related bacteremia, enterococcal sepsis, klebsiella bacteremia, streptococcal bacteremia, septic shock, staphylococcal bacteremia, streptococcal sepsis.
- Motor dysfunction includes akathisia, dyskinesia, dysphonia, hypertonia, muscle spasms, muscle twitching, muscular weakness, restless legs syndrome.
- Tremor includes head titubation, intention tremor, resting tremor, tremor.
- Aphasias include aphasia, dysarthria, slow speech, speech disorder.
- Delirium includes agitation, delirium, disorientation, hallucination, hallucination auditory, hallucination visual, restlessnes.
- Pulmonary edema includes pulmonary congestion and pulmonary edema.
- Thrombosis includes deep vein thrombosis, device related thrombosis, embolism, pulmonary embolism, thrombosis, thrombosis in device.

Laboratory Abnormalities:

Table 4 presents the most common Grade 3 or 4 laboratory abnormalities, based on laboratory data, occurring in at least 10% of patients.

**Table 4: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in at Least 10% of Patients Treated in the KarMMa-3 Study**

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>N=222</th>
<th>N=128</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3 or 4 (%)</td>
<td>Grade 3 or 4 (%)</td>
</tr>
<tr>
<td>Lymphocyte decreased</td>
<td>98</td>
<td>78</td>
</tr>
<tr>
<td>Leukocyte decreased</td>
<td>96</td>
<td>64</td>
</tr>
<tr>
<td>Neutrophil decreased</td>
<td>96</td>
<td>72</td>
</tr>
<tr>
<td>Platelet decreased</td>
<td>59</td>
<td>46</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>52</td>
<td>45</td>
</tr>
<tr>
<td>Phosphate decreased</td>
<td>45</td>
<td>30</td>
</tr>
<tr>
<td>Triglyceride increased</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Sodium decreased</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Gamma-glutamyltransferase increased</td>
<td>10</td>
<td>6</td>
</tr>
</tbody>
</table>

CAR=chimeric antigen receptor; CTCAE = Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

Other clinically important Grade 3 or 4 laboratory abnormalities (based on laboratory data) that occurred in less than 10% of patients treated with ABECMA include the following: aspartate aminotransferase increased, potassium decreased, albumin decreased, alkaline phosphatase increased, calcium decreased, glucose increased, activated partial thromboplastin time increased (seconds), fibrinogen decreased, bilirubin increased and hypomagnesemia.

**KarMMa Study**

The safety data described in this section reflect the exposure to ABECMA in the KarMMa study, in which 127 patients with relapsed/refractory multiple myeloma received ABECMA across a dose range of 150 to 518 x 10^6 CAR-positive T cells [see Clinical Studies (14)]. Patients with a history of CNS disease (such as seizure or cerebrovascular ischemia) or requiring ongoing treatment with chronic immunosuppression were excluded. The Eastern Cooperative Oncology Group (ECOG) performance status at baseline was 61 years (range: 33 to 78 years); 35% were 65 years or older, and 60% were men.

The most common (greater than or equal to 10%) Grade 3 or 4 laboratory abnormal adverse reactions were febrile neutropenia (16%) and infections – pathogen unspecified (15%).

The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) included CRS, infections – pathogen unspecified, fatigue, muscle spasms, 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. The most common nonlaboratory (greater than or equal to 5%) serious adverse reactions included CRS (18%), general physical health deterioration (10%), pneumonia (12%), infections-pathogen unspecified (19%), viral infections (9%), sepsis (7%), and febrile neutropenia (6%). Fatal adverse reactions occurred in 6%.

Table 5 summarizes the adverse reactions that occurred in at least 10% of patients treated with ABECMA. Table 6 describes the most common Grade 3 or 4 laboratory abnormalities.

**Table 5: Adverse Reactions Observed in at Least 10% of Patients Treated with ABECMA in the KarMMa Study**

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Grade 3 or 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile neutropenia</td>
<td>16</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>19</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>35</td>
</tr>
<tr>
<td>Nausea</td>
<td>29</td>
</tr>
<tr>
<td>Constipation</td>
<td>16</td>
</tr>
<tr>
<td>Vomiting</td>
<td>15</td>
</tr>
<tr>
<td>Oral pain</td>
<td>12</td>
</tr>
<tr>
<td>Respiratory, thoracic, and mediastinal disorders</td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>10</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>13</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>14</td>
</tr>
<tr>
<td>Xerosis</td>
<td>11</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>11</td>
</tr>
</tbody>
</table>

(Continued)
Other clinically important adverse reactions that occurred in less than 10% of patients treated with ABECMA include the following:

- **Blood and lymphatic system disorders:** coagulopathy\(^a\) (9%)
- **Cardiac disorders:** atrial fibrillation (4.7%), cardiomyopathy\(^b\) (1.6%)
- **Gastrointestinal disorders:** gastrointestinal hemorrhage\(^c\) (3.1%)
- **Immune system disorders:** hemophagocytic lymphohistiocytosis (3.1%)
- **Infections and infestations:** fungal infections (8%), sepsis\(^d\) (9%)
- **Nervous system disorders:** aphasia\(^e\) (7%), ataxia\(^f\) (3.1%), paresis\(^g\) (2.4%), seizure (1.6%)
- **Psychiatric disorders:** delirium\(^h\) (6%)
- **Respiratory, thoracic, and mediastinal disorders:** hypoxia (2.4%), pulmonary edema (2.4%)
- **Vascular disorders:** thrombosis\(^i\) (3.1%)

\(^a\) Coagulopathy includes activated partial thromboplastin time prolonged, anticoagulation drug level above therapeutic, disseminated intravascular coagulation, international normalized ratio increased.

\(^b\) Cardiomyopathy includes stress cardiomyopathy, ventricular hypertrophy.

\(^c\) Gastrointestinal hemorrhage includes gastrointestinal hemorrhage, hemorrhoidal hemorrhage, melena.

\(^d\) Sepsis includes bacteremia, enterococcal bacteremia, Escherichia bacterium, sepsis, septic shock, Serratia bacterium, streptococcal bacteremia.

\(^e\) Aphasia includes aphasia, dysarthria.

\(^f\) Ataxia includes ataxia, gait disturbance, Romberg test positive.

\(^g\) Paresis includes cranial nerve disorder, hemiparesis.

\(^h\) Delirium includes delirium, disorientation, hallucination.

\(^i\) Thrombosis includes deep vein thrombosis, jugular vein thrombosis, portal vein thrombosis, pulmonary embolism.

---

**Table 5: Adverse Reactions Observed in at Least 10% of Patients Treated with ABECMA in the KarMMA Study**

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Dose (150 to 450 x 10^6 CAR-Positive T cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3 or 4 (%)</td>
</tr>
<tr>
<td>Neutrophil decreased</td>
<td>96</td>
</tr>
<tr>
<td>Leukocyte decreased</td>
<td>96</td>
</tr>
<tr>
<td>Lymphocyte decreased</td>
<td>92</td>
</tr>
<tr>
<td>Platelet decreased</td>
<td>63</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>63</td>
</tr>
<tr>
<td>Phosphate decreased</td>
<td>45</td>
</tr>
<tr>
<td>Sodium decreased</td>
<td>10</td>
</tr>
<tr>
<td>aPTT increased (seconds)</td>
<td>10</td>
</tr>
</tbody>
</table>

\(^a\) NCI CTCAE = Common Terminology Criteria for Adverse Events version 4.03.

---

8 Laboratory Abnormalities

6.3 Postmarketing Experience

Because adverse events to marketed products are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure.

The following adverse event has been identified during postmarketing use of ABECMA:

- **Nervous system disorders:** Immune effector cell-associated neurotoxicity syndrome (ICANS). The following adverse event has been identified during postmarketing use of BCMA- or CD19-directed genetically modified autologous T cell immunotherapies:

- **Neoplasms:** T cell malignancies.

7 DRUG INTERACTIONS

Drug/Laboratory Test Interactions

HIV and the lentivirus used to make ABECMA 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 ABECMA.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

**Risk Summary**

There are no available data with ABECMA use in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with ABECMA to assess whether it can cause fetal harm when administered to a pregnant woman.

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 plasma cell aplasia or hypogammaglobulinemia. Therefore, ABECMA is not recommended for women who are pregnant, and pregnancy after ABECMA infusion should be discussed with the treating physician. Assess immunoglobulin levels in newborns of mothers treated with ABECMA.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. The estimated background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

---

**Table 6: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in at Least 10% of Patients Treated with ABECMA in the KarMMA Study**

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Dose (150 to 450 x 10^6 CAR-Positive T cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3 or 4 (%)</td>
</tr>
<tr>
<td>Neutrophil decreased</td>
<td>96</td>
</tr>
<tr>
<td>Leukocyte decreased</td>
<td>96</td>
</tr>
<tr>
<td>Lymphocyte decreased</td>
<td>92</td>
</tr>
<tr>
<td>Platelet decreased</td>
<td>63</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>63</td>
</tr>
<tr>
<td>Phosphate decreased</td>
<td>45</td>
</tr>
<tr>
<td>Sodium decreased</td>
<td>10</td>
</tr>
<tr>
<td>aPTT increased (seconds)</td>
<td>10</td>
</tr>
</tbody>
</table>

\(^a\) NCI CTCAE = Common Terminology Criteria for Adverse Events version 4.03.

**CTCAE = Common Terminology Criteria for Adverse Events; NCI = National Cancer Institute.**
2.1 Mechanism of Action
ABECMA is a chimeric antigen receptor (CAR)-positive T cell therapy targeting B-cell maturation antigen (BCMA), which is expressed on the surface of normal and malignant plasma cells. The CAR construct includes an anti-BCMA scFv-targeting domain for antigen specificity, a transmembrane domain, a CD3-zeta T cell activation domain, and a 4–1BB costimulatory domain. Antigen-specific activation of ABECMA results in CAR-positive T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells.

2.2 Pharmacodynamics
Following ABECMA infusion, pharmacodynamic responses of CAR activation and anti-tumor efficacy were evaluated. Peak elevation of plasma cytokines, chemokines, and soluble immune mediators occurred within 14 days of ABECMA infusion and returned to baseline levels within one month.

Rapid decreases in tumor markers associated with clinical response, including serum levels of soluble BCMA, and bone marrow CD138+ cells, as well as minimal residual disease (MRD) negative responses, were observed within the first month following ABECMA infusion.

12.3 Pharmacokinetics
ABECMA transgene levels were positively associated with objective tumor response (partial response or better). Among patients who received ABECMA in KarMMa, the median $C_{\text{max}}$ levels in responders (N = 72) were approximately 4.6-fold higher than the corresponding levels in non-responders (N = 27). Median AUC$_{0-28\text{days}}$ in responders (N = 72) was approximately 5.6-fold higher than non-responders (N = 26). Among patients who received ABECMA in KarMMa-3, the median $C_{\text{max}}$ levels in responders (N = 172) were approximately 6.5-fold higher compared to the corresponding levels in non-responders (N = 35). Median AUC$_{0-28\text{days}}$ in responders (N = 172) was approximately 6.1-fold higher than non-responders (N = 33).

Tocilizumab or Siltuximab and Corticosteroid Use
Some patients required tocilizumab or siltuximab and/or corticosteroid for the management of CRS. ABECMA can continue to expand and persist following tocilizumab or siltuximab or corticosteroid administration [see Warnings and Precautions (5.2)].

In KarMMa patients with CRS treated with tocilizumab had higher ABECMA cellular expansion levels, as measured by 1.3-fold and 1.6-fold higher median $C_{\text{max}}$ (N = 67) and AUC$_{0-28\text{days}}$ (N = 66), respectively, compared to patients who did not receive tocilizumab (N = 59 for $C_{\text{max}}$ and N = 58 for AUC$_{0-28\text{days}}$).

Patients with CRS treated with corticosteroids had higher ABECMA cellular expansion levels, as measured by 1.7-fold and 2.2-fold higher median $C_{\text{max}}$ (N = 18) and AUC$_{0-28\text{days}}$ (N = 18), respectively, compared to patients who did not receive corticosteroids (N = 108 for $C_{\text{max}}$ and N = 106 for AUC$_{0-28\text{days}}$).

Similar trend was observed in KarMMa-3.

Specific Populations
Geriatric
Age (range: 30 to 81 years) had no significant impact on expansion parameters [see Use in Special Populations (8.2)].

Pediatric
The pharmacokinetics of ABECMA in patients less than 18 years of age have not been evaluated.

Patients with Hepatic/Renal Impairment
Hepatic and renal impairment studies of ABECMA were not conducted.

Patients with Other Intrinsic Factors
Gender, race, and ethnicity had no significant impact on ABECMA expansion parameters. Patients with lower body weight had higher expansion. Due to high variability in pharmacokinetic cellular expansion, the overall effect of weight on the pharmacokinetics of ABECMA is considered to be not clinically relevant.
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Genotoxicity assays and carcinogenicity studies in rodents were not performed for ABECMA.

In vitro expansion studies with CAR-positive T cells (ABECMA) from 5 patients and 2 healthy donor drug product lots showed no evidence for transformation and/or immortalization of T cells. A genomic insertion site analysis of the lentiviral vector was performed on ABECMA samples from twenty (20) individual patient donors. There was no evidence for preferential integration near genes of concern or preferential outgrowth of cells harboring integration sites of concern.

No studies on the effects of ABECMA on fertility have been conducted.

14 CLINICAL STUDIES

Relapsed/Refractory Multiple Myeloma After Two to Four Prior Lines of Therapy

Efficacy of ABECMA was evaluated in KarMMa-3 (NCT03651128), an open-label, multicenter, randomized, controlled study in adult patients with relapsed and refractory multiple myeloma who had received two to four prior anti-myeloma therapies including an immunomodulatory agent, a proteasome inhibitor and daratumumab, and were refractory to the most recent prior anti-myeloma regimen. The study included patients who achieved a response (minimal response or better) to at least 1 prior treatment regimen and had ECOG performance status of 0 or 1. The study excluded patients with serum creatinine clearance <45 mL/min, serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >2.5 times upper limit of normal, and left ventricular ejection fraction (LVEF) <45%. Patients were also excluded if absolute neutrophil count <1000/µL and platelet count <50,000/µL in patients in whom ≥50% of bone marrow nucleated cells are plasma cells and platelet count <50,000/µL in patients in whom ≥50% of bone marrow nucleated cells are plasma cells.

In total, 386 patients were randomized 2:1 to receive either ABECMA (N = 254) or standard regimens (N = 132). The standard regimens consisted of daratumumab, pomalidomide, (30 mg/m2 IV infusion daily for 3 days) starting 5 days prior to the target infusion date of ABECMA. Up to 1 cycle of DPd, DVd, IRd, Kd or EPd bridging therapy, dependent on the patient’s most recent antimyeloma treatment regimen, was permitted for disease control contingent upon the patient’s most recent antimyeloma treatment. Randomization was stratified by age, number of prior antimyeloma regimens, and presence of high-risk cytogenetics abnormalities.

Patients randomized to ABECMA were to receive lymphodepleting chemotherapy consisting of cyclophosphamide (300 mg/m² IV infusion daily for 3 days) and fludarabine (30 mg/m² IV infusion daily for 3 days) starting 5 days prior to the target infusion date of ABECMA. Up to 1 cycle of DPd, DVd, IRd, Kd or EPd bridging therapy, dependent on the patient’s most recent antimyeloma treatment regimen, was permitted for disease control between apheresis and until 14 days before the start of lymphodepleting chemotherapy. Of the 254 patients randomized to receive ABECMA, 249 (98%) patients underwent leukapheresis:

- Five (2%) patients did not receive leukapheresis due to patient withdrawal (n = 2), adverse event (n = 1) or failure to meet lymphodepleting chemotherapy treatment criteria (n = 2).
- Twenty-four (10%) patients did not receive ABECMA either due to death (n = 4), adverse event (n = 4), physician decision (n = 7), failure to meet lymphodepleting chemotherapy treatment criteria (n = 6) or inability to manufacture product (n = 3).
- Three (1%) patients received CAR-positive T cells that did not meet product release specifications for ABECMA (non-conforming product; n = 3).

The overall manufacturing failure rate for patients who underwent leukapheresis was 2.4% (6 out of 249 patients). Of these 6 patients, 3 received CAR positive T cells that did not meet product release specifications for ABECMA, and in 3 patients there was an inability to manufacture ABECMA.

Most patients (85%) treated with ABECMA received bridging therapy for control of their multiple myeloma during the manufacturing process. The median time from leukapheresis to product availability was 35 days (range: 24 to 102 days). In overall study population, the median age was 63 years (range: 30 to 83 years), 61% were male, 65% were white, 9.3% were black and 3.1% were Asian. Most patients (80%) were Revised International Staging System (R-ISS) Stage I or II. High-risk cytogenetics [presence of t(4;14), (14;16) and 17p13 del] were present in 42% of patients. Twenty-four percent of patients had presence of extramedullary disease.

The median number of prior lines of therapy was 3 (range: 2 to 4). Thirty percent had received 2 prior lines, 37% had received 3 prior lines of therapy and 32% had received 4 prior lines of therapy. Ninety-five percent were refractory to an anti-CD38 monoclonal antibody. Sixty-six percent were triple class refractory (refractory to a PI, an IMiD and an anti-CD38 monoclonal antibody) and 5% were penta-drug-refractory (refractory to 2 PIs, 2 IMiD agents, and an anti-CD38 monoclonal antibody). Eighty-five percent of patients had received prior autologous stem cell transplantation.

The primary efficacy measure was progression free survival (PFS) as determined by Independent Review Committee (IRC) based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. Other efficacy measures included overall response rate (ORR) and overall survival (OS). Efficacy results are summarized in Table 8, and Kaplan-Meier curve for PFS is provided in Figure 2. The estimated median duration of follow-up at the primary PFS analysis was 15.9 months (95% CI: 14.1, 18.0).

Table 8: Summary of Efficacy Results from KarMMa-3 (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th></th>
<th>ABECMA Arm (N = 254)</th>
<th>Standard Regimens Arm (N = 132)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression Free Survival (PFS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of events, n (%)</td>
<td>149 (59)</td>
<td>93 (70)</td>
</tr>
<tr>
<td>Median, months [95% CI]a</td>
<td>13.3 [11.8, 16.1]</td>
<td>4.4 [3.4, 5.9]</td>
</tr>
<tr>
<td>Hazard Ratio [95% CI]b</td>
<td>0.49 [0.38, 0.64]</td>
<td></td>
</tr>
<tr>
<td>One-sided p-valuec</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

ORR, n (%)

- sCR 90 (35) 6 (4.5)
- CR or better (sCR+CR) 98 (39) 7 (5)
- sCR 90 (35) 6 (4.5)
- CR 8 (3.1) 1 (0.8)
- VGPR 55 (22) 13 (10)
- PR 28 (11) 35 (27)

CI = confidence interval; CR = complete response; MRD = minimal residual disease; PR = partial response; sCR = stringent complete response; VGPR = very good partial response.

a Kaplan-Meier estimate.
b Based on stratified univariate Cox proportional hazards model.
c One-sided p-value is based on stratified log-rank test.
de Two-sided Wald confidence interval.
e One-sided p-value from Cochran-Mantel-Haenszel (CMH) test stratified by stratification factors.

Figure 2: Kaplan-Meier Plot of IRC-Assessed Progression Free Survival (Intent-to-Treat Analysis)

Number at Risk

ABECMA 254 206 178 149 110 62 40 22 14 4 2 0
Standard Regimen 132 75 42 32 25 13 10 7 6 2 1 0

Data cutoff date: April 18, 2022.

In the ABECMA arm, the median duration of response (DOR) was 14.8 months (95% CI: 12.0, 16.6) in patients with partial response (PR) or better. In those patients with CR or better, the median DOR was 20 months (95% CI: 15.8, 24.3).

A higher proportion of patients in the ABECMA arm compared to the standard regimen’s arm died within the first 9 months of randomization as shown in Figure 3.
ABECMA® (idecabtagene vicleucel)

21
24
30
42
48
18
27
12
ABECMA® (idecabtagene vicleucel) ABECMA® (idecabtagene vicleucel)

were previously exposed was permitted for disease control between apheresis and until CAR-positive T cell dose cohorts:

and platelet count <50,000/mm3. Patients had measurable disease by IMWG 2016 criteria alanine aminotransferase >2.5 times upper limit of normal, and left ventricular ejection antibody. The study included patients with ECOG performance status of 0 or 1. The study an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal single-arm, multicenter study in adult patients with relapsed and refractory multiple Myeloma After Three or More Prior Lines of Therapy Relapsed/Refractory Multiple Myeloma After Three or More Prior Lines of Therapy Efficacy of ABECMA was evaluated in KarMMa (NCT03361748), an open-label, single-arm, multicenter study in adult patients with relapsed and refractory multiple myeloma who had received at least 3 prior lines of antmyeloma therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. The study included patients with ECOG performance status of 0 or 1. The 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%. Patients were also excluded if absolute neutrophil count <1000 cells/mm³ and platelet count <50,000/mm³. Patients had measurable disease by IMWG 2016 criteria at enrollment. Bridging therapy with alkylating agents, corticosteroids, immunomodulatory agents, proteasome inhibitors, and/or anti-CD38 monoclonal antibodies to which patients were previously exposed was permitted for disease control between apheresis and until 14 days before the start of lymphodepleting chemotherapy.

Lymphodepleting chemotherapy consisted of cyclophosphamide (300 mg/m² IV infusion daily for 3 days) and fludarabine (30 mg/m² IV infusion daily for 3 days) starting 5 days prior to the target infusion date of ABECMA. Fludarabine was dose reduced for renal insufficiency. Patients were hospitalized for 14 days after ABECMA infusion to monitor for potential CRS, HLH/MAS, and neurotoxicity. Of the 135 patients who underwent leukapheresis for 300 x 10⁶ and 450 x 10⁶ CAR-positive T cell dose cohorts:

• 11 (8%) did not receive the CAR-positive T cells either due to death (n=2), adverse event (n=1), disease progression (n=1), consent withdrawal (n=3), physician decision (n=3), or inability to manufacture product [manufacturing failure (n=1)]. Two patients died after receiving lymphodepletion and prior to receiving ABECMA. Deaths were from septic shock and general physical health deterioration.

• 24 (18%) either received ABECMA outside of the 300 to 460 x 10⁶ CAR-positive T cells dose range (n=23) or received CAR-positive T cells that did not meet product release specifications for ABECMA (non-conforming product; n=1).

• The efficacy evaluable population consists of the 100 patients (74%) who received ABECMA in the dose range of 300 to 460 x 10⁶ CAR-positive T cells.

The overall manufacturing failure rate for patients who underwent leukapheresis for the 300 x 10⁶ and 450 x 10⁶ CAR-positive T cell dose cohorts was 1.5% (2 out of 135 patients). Of these 2 patients, one received CAR-positive T cells that did not meet product release specifications for ABECMA, and in one patient there was an inability to manufacture ABECMA.

Of the 100 patients in the efficacy evaluable population, the median age was 62 years (range: 33 to 78 years), 60% were male, 78% were white, 8% were black, and 2% were Asian. Most patients (78%) were International Staging System (ISS) Stage I or II. High-risk cytogenetics (presence of t(4:14), t(14:16), and 17p13 del) were present in 37% of patients. Thirty-six percent of the patients had presence of extramedullary disease.

The median number of prior lines of therapy was 6 (range: 3 to 16), and 88% of the patients received 4 or more prior lines of therapy. Ninety-five percent of the patients were refractory to an anti-CD38 monoclonal antibody. Eighty-five percent were triple class refractory (refractory to a proteasome inhibitor [PI], an immunomodulatory drug [IMiD], and an anti-CD38 monoclonal antibody), and 26% were penta-refractory (refractory to 2 PIs, 2 IMiD agents, and an anti-CD38 monoclonal antibody). Ninety-two percent had received prior autologous stem cell transplantation.

Most patients (87%) treated with ABECMA received bridging therapy for control of their multiple myeloma during the manufacturing process. The median time from leukapheresis to product availability was 33 days (range: 26 to 49 days).

Efficacy was established on the basis of overall response rate (ORR), complete response (CR) rate, and duration of response (DOR), as assessed by the Independent Response committee (IRC) based on the International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma.

Efficacy results for the dose range of 300 to 460 x 10⁶ CAR-positive T cells are shown in Table 9 and Table 10, and the DOR results are shown in Table 11. The median time to first response was 30 days (range: 15 to 88 days).

Table 9: Summary of Efficacy Based on Independent Response Committee Review According to IMWG Criteria (KarMMa Study)

<table>
<thead>
<tr>
<th>Overall Response Rate</th>
<th>ABECMA-Treated Population (300 to 460 x 10⁶ CAR-Positive T Cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(sCR=VGPR+PR), n (%)</td>
<td>72 (72)</td>
</tr>
<tr>
<td>95% CI (96, 81)</td>
<td></td>
</tr>
<tr>
<td>sCR, n (%)</td>
<td>28 (28)</td>
</tr>
<tr>
<td>95% CI (19, 38)</td>
<td></td>
</tr>
<tr>
<td>VGPR, n (%)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>95% CI (17, 35)</td>
<td></td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>19 (19)</td>
</tr>
<tr>
<td>95% CI (12, 28)</td>
<td></td>
</tr>
</tbody>
</table>

Table 10: MRD Negativity Rate in the KarMMa Study

<table>
<thead>
<tr>
<th>MRD—negativity ratea in all treated patients (n=100)</th>
<th>21 (21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% CI (94, 97)</td>
<td>13, 30</td>
</tr>
<tr>
<td>MRD—negativity rate in patients achieving CR or sCR status (n=100)</td>
<td>21 (75)</td>
</tr>
<tr>
<td>95% CI (90, 95)</td>
<td>55, 89</td>
</tr>
</tbody>
</table>

Table 11: Duration of Response in the KarMMa Study

<table>
<thead>
<tr>
<th>Duration of Responsea, b (PR or Better)</th>
<th>ABECMA-Treated Population (300 to 460 x 10⁶ CAR-Positive T Cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>72</td>
</tr>
<tr>
<td>Median (months)</td>
<td>11.0</td>
</tr>
<tr>
<td>95% CI</td>
<td>10.3, 11.4</td>
</tr>
<tr>
<td>Duration of Responsea for sCR</td>
<td>28</td>
</tr>
<tr>
<td>Median (months)</td>
<td>19.0</td>
</tr>
<tr>
<td>95% CI</td>
<td>11.4, NE</td>
</tr>
<tr>
<td>Median follow-up for duration of response (DOR)</td>
<td>10.7 months</td>
</tr>
</tbody>
</table>

a MRD negativity was defined as the proportion of patients with CR or stringent CR who are MRD negative at any timepoint within 3 months prior to achieving CR or stringent CR until the time of progression or death.

b Clopper-Pearson exact CI.

c Based on a threshold of 10⁻⁶ using ClonoSEQ, a next-generation sequencing assay (NGS).

PR = partial response; sCR = stringent complete response; VGPR = very good partial response.

b Median and 95% CI are based on Kaplan-Meier estimation.
Response durations were longer in patients who achieved a stringent CR as compared to patients with a PR or VGPR (Table 11). Of the 28 patients who achieved a stringent CR, it is estimated that 65% (95% CI: 42%, 81%) had a remission lasting at least 12 months.

The median duration of response for VGPR patients (n = 25) was 11.1 months (95% CI: 8.7, 11.3).

The median duration of response for PR patients (n = 19) was 4.0 months (95% CI: 2.7, 7.2).

Within the recommended dose of 300 to 460 x 10^6 CAR-positive T cells, a dose-response relationship was observed with higher ORR and sCR rate in patients who received 440 to 460 x 10^6 compared to 300 to 340 x 10^6 CAR-positive T cells. Overall response rate of 79% (95% CI: 65%, 90%) and sCR rate of 31% (95% CI: 19%, 46%) was observed with 440 to 460 x 10^6 CAR-positive T cells. Overall response rate of 65% (95% CI: 51%, 78%) with sCR rate of 25% (95% CI: 14%, 39%) was observed in 300 to 340 x 10^6 CAR-positive T cells.

One hundred and thirty-five patients underwent leukapheresis. Fifteen out of the 23 patients who received treatment outside of the recommended dose range of 300 to 460 x 10^6 CAR-positive T cells experienced a response in addition to the responses noted in Table 9. The IRC assessed overall response in the leukapheresis population (n = 135) was 64% (95% CI: 56%, 72%) with stringent CR rate of 24% (95% CI: 17%, 32%), VGPR rate of 21% (95% CI: 14%, 29%), and PR rate of 20% (95% CI: 14%, 28%).

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

ABECMA® is supplied in one or more infusion bags (see below) containing a frozen suspension of genetically modified autologous T cells in 5% DMSO.

Each infusion bag of ABECMA® is individually packed in a metal cassette. ABECMA® is stored in the vapor phase of liquid nitrogen and supplied in a liquid nitrogen dry vapor shipper. An RFI Certificate is affixed inside the shipper.

- 50 mL infusion bag and metal cassette (NDC 59572-515-01)
- 250 mL infusion bag and metal cassette (NDC 59572-515-02)
- 500 mL infusion bag and metal cassette (NDC 59572-515-03)

Match the identity of the patient with the patient identifiers on the cassette(s) and infusion bag(s) upon receipt.

Store ABECMA® frozen in the vapor phase of liquid nitrogen (less than or equal to minus 130°C).

Thaw ABECMA® prior to infusion [see Dosage and Administration (2.2)].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise patients that the risk of manufacturing failure is 2.1% [8/384 in the clinical studies].

In case of a manufacturing failure, a second manufacturing of ABECMA may be attempted. In addition, while the patient awaits the product, additional anticancer treatment (not the lymphodepletion) may be necessary and may increase the risk of adverse events during the pre-infusion period, which could delay or prevent the administration of ABECMA.

Inform patients of the risk of early death: In a clinical study, a higher proportion of patients experienced death within the first 9 months from randomization in the ABECMA arm compared to the standard regimens arm. This higher rate of early death was mainly observed before receiving ABECMA with the main reason being progression of multiple myeloma. There was also an increase in the rate of death from adverse events after ABECMA.

Advise patients to seek immediate attention for any of the following:

- Cytokine Release Syndrome (CRS): Signs or symptoms associated with CRS, including fever, hypotension, tachycardia, chills, hypoxia, headache, and fatigue [see Dosage and Administration (2.3), Warnings and Precautions (5.2), and Adverse Reactions (6.1)].
- Neurologic Toxicities: Signs or symptoms associated with neurologic events, including encephalopathy, confusion, seizures, tremor, aphasia, delirium, and somnolence [see Dosage and Administration (2.3), Warnings and Precautions (5.3), and Adverse Reactions (6.1)].
- Infections: Signs or symptoms associated with infection [see Warnings and Precautions (5.7) and Adverse Reactions (6.1)].
- Prolonged Cytopenias: Signs or symptoms associated with bone marrow suppression, including neutropenia, anemia, thrombocytopenia, or febrile neutropenia [see Warnings and Precautions (5.8) and Adverse Reactions (6.1)].
- Secondary malignancies: Secondary malignancies, including T cell malignancies, have occurred [see Boxed Warning, Warnings and Precautions (5.10), Adverse Reactions (6.3)].

Advise patients for the need to:

- Contact Bristol-Myers Squibb at 1-888-805-4555 if they are diagnosed with a secondary malignancy [see Warnings and Precautions (5.10)].
- Have periodic monitoring of blood counts before and after ABECMA infusion [see Warnings and Precautions (5.8)].
- Refrain from driving or operating heavy or potentially dangerous machines until at least 8 weeks after ABECMA administration [see Warnings and Precautions (5.11)].

Manufactured by: Celgene Corporation, a Bristol-Myers Squibb Company
556 Morris Avenue
Summit, NJ 07901
U.S. License No. 2252

Marketed by:
Celgene Corporation, a Bristol-Myers Squibb Company (Summit, NJ 07901), and 2seventy bio, Inc. (Cambridge, MA 02142).

ABECMA® is a trademark of Celgene Corporation, a Bristol-Myers Squibb Company.
ABEPI.003/MG.002
### What is the most important information I should know about ABECMA?

ABECMA may cause side effects that are life-threatening and can lead to death. Call your healthcare provider or get emergency help right away if you get any of the following:

- difficulty breathing
- fever (100.4°F/38°C or higher)
- chills/shivering
- confusion
- dizziness or lightheadedness
- shaking or twitching (tremor)
- fast or irregular heartbeat
- severe fatigue
- severe nausea, vomiting, diarrhea

It is important that you tell your healthcare providers that you have received ABECMA and to show them your ABECMA Patient Wallet Card. Your healthcare provider may give you other medicines to treat your side effects.

### What is ABECMA?

ABECMA is for the treatment of multiple myeloma in patients who have received at least two kinds of treatment regimens that have not worked or have stopped working. ABECMA is a medicine made from your own white blood cells; the cells are genetically modified to recognize and attack your multiple myeloma cells.

### How will I receive ABECMA?

ABECMA is made from your own white blood cells, so your blood will be collected by a process called “leukapheresis” (LOO-kuh-feh-REE-sis).

Your blood cells will be sent to a manufacturing center to make your ABECMA. Based on clinical trial experience, it takes about 4 weeks from the time your cells are received at the manufacturing site and are available to be shipped back to your healthcare provider, but the time may vary.

Before you get ABECMA, your healthcare provider will give you chemotherapy for 3 days to prepare your body.

When your ABECMA is ready, your healthcare provider will give ABECMA to you through a catheter (tube) placed into your vein (intravenous infusion). Your dose of ABECMA may be given in one or more infusion bags. The infusion usually takes up to 30 minutes for each infusion bag.

You will be monitored at the certified healthcare facility where you received your treatment daily for at least 7 days after the infusion.

You should plan to stay within 2 hours of this location for at least 4 weeks after getting ABECMA. Your healthcare provider will check to see that your treatment is working and help you with any side effects that may occur.

### What should I avoid after receiving ABECMA?

- Do not drive, operate heavy machinery, or do other activities that could be dangerous if you are not mentally alert, for at least 8 weeks after you get ABECMA. This is because the treatment can cause temporary memory and coordination problems, sleepiness, confusion, dizziness, and seizures.
- Do not donate blood, organs, tissues, or cells for transplantation.

### What are the possible or reasonably likely side effects of ABECMA?

The most common side effects of ABECMA are:

- fatigue
- fever (100.4°F/38°C or higher)
In a study comparing ABECMA to standard regimen, a higher proportion of patients experienced death within the first 9 months from randomization in the ABECMA arm compared to the standard regimen arm. This higher rate of early death was mainly observed before receiving ABECMA with the main reason being progression of multiple myeloma. There was also an increase in the rate of death from adverse events after ABECMA.

ABECMA can cause a very common side effect called cytokine release syndrome or CRS, which can be severe or fatal. Symptoms of CRS include fever, difficulty breathing, dizziness or light-headedness, nausea, headache, fast heartbeat, low blood pressure, or fatigue. Tell your healthcare provider right away if you develop fever or any of these other symptoms after receiving ABECMA.

ABECMA can increase the risk of life-threatening infections that may lead to death. Tell your healthcare provider right away if you develop fever, chills, or any signs or symptoms of an infection.

ABECMA can lower one or more types of your blood cells (red blood cells, white blood cells, or platelets), which may make you feel weak or tired or increase your risk of severe infection or bleeding. After treatment, your healthcare provider will test your blood to check for this. Tell your healthcare provider right away if you get a fever, are feeling tired, or have bruising or bleeding.

ABECMA may increase your risk of getting cancers including certain types of blood cancers. Your healthcare provider should monitor you for this.

Having ABECMA in your blood may cause a false-positive human immunodeficiency virus (HIV) test result by some commercial tests.

These are not all the possible side effects of ABECMA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of ABECMA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about ABECMA, talk with your healthcare provider. You can ask your healthcare provider for information about ABECMA that is written for health professionals.

For more information, go to ABECMA.com or call 1-888-805-4555.

Manufactured by: Celgene Corporation, a Bristol-Myers Squibb Company, 556 Morris Avenue, Summit, NJ 07901.

Marketed by: Celgene Corporation, a Bristol-Myers Squibb Company (Summit, NJ 07901), and 2seventy bio, Inc. (Cambridge, MA 02142).

ABECMA® is a trademark of Celgene Corporation, a Bristol-Myers Squibb Company.

ABEMG002  4/2024

This Medication Guide has been approved by the U.S. Food and Drug Administration.