

# Clinician's Guide to ABECMA<sup>®</sup> CAR T Cell Therapy Process

**Includes information on the ABECMA process, patient eligibility, leukapheresis, manufacturing, and adverse events**

2L=second-line; CAR=chimeric antigen receptor.

## INDICATION

ABECMA (idecabtagene vicleucel) 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.

## IMPORTANT SAFETY INFORMATION

### WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA and SECONDARY HEMATOLOGICAL 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.
- 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.
- 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.
- Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA.

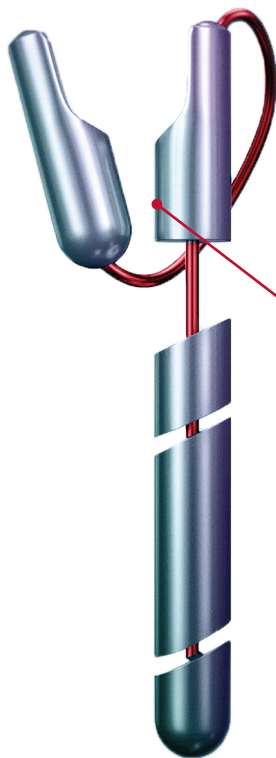
Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

# ABECMA<sup>®</sup> Is the First CAR T Cell Therapy for RRMM<sup>1</sup>



## A personalized immune cell therapy that targets BCMA with a one-time infusion<sup>1\*</sup>

ABECMA consists of T cells transduced with a CAR lentiviral vector.



The CAR construct includes an extracellular **scFv-targeting domain that binds specifically to BCMA**, a cell-surface antigen expressed at significantly higher levels on malignant plasma cells of MM.<sup>1,2†</sup>

### TARGETING BCMA

BCMA expression is largely restricted to plasma cells and is uniquely overexpressed on myeloma cells, making BCMA a promising target antigen.<sup>1,2†</sup>

Following ABECMA infusion, the CAR-positive cells proliferate and undergo rapid multilog expansion followed by a bi-exponential decline. ABECMA can persist in peripheral blood for up to 1 year post infusion.<sup>1</sup>

\*Treatment process includes leukapheresis, manufacturing, administration, and adverse event monitoring. A single dose of ABECMA contains a cell suspension of 300 to 510 x 10<sup>6</sup> CAR-positive T cells in 1 or more infusion bags.<sup>1</sup>

†BCMA is expressed both on normal and malignant plasma cells.<sup>2</sup>

BCMA=B-cell maturation antigen; MM=multiple myeloma; RRMM=relapsed/refractory multiple myeloma; scFv=single-chain variable fragment.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### Warnings and Precautions:

**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%). 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.

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## IMPORTANT SAFETY INFORMATION (cont'd)

**Cytokine Release Syndrome (CRS):** CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including  $\geq$  Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) 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 63 days). In the pooled studies, the rate of  $\geq$ Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10<sup>6</sup> CAR-positive T cells.

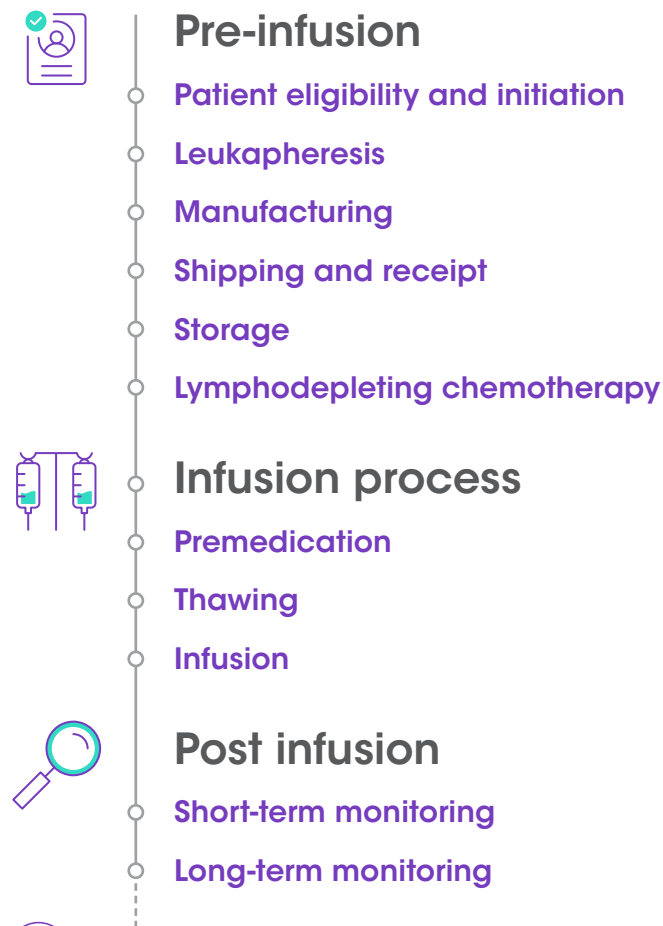
The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

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## The ABECMA<sup>®</sup> Process

### An overview of the ABECMA process<sup>1</sup>



At any point during the ABECMA process, you can visit the Scheduling and Apheresis Portal at [www.CT360.com](http://www.CT360.com) for appointment and product status information.

### IMPORTANT SAFETY INFORMATION (cont'd)

**Cytokine Release Syndrome (CRS) (cont'd):** 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 10<sup>6</sup> CAR-positive T cells, 76% (54/71) of patients received 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 10<sup>6</sup> 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.

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## Patient Eligibility and Initiation

### Determining eligibility for ABECMA<sup>1,3</sup>

Eligible adult patients include those with RRMM after 2L who are:

- Triple-class exposed\* who have received 2 or more prior therapies
- Have received 2 kinds of treatment regimens that include an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody
- Clinical fitness (eg, good performance status and adequate organ function)

### Pivotal trial population<sup>1,3</sup>

KarMMa-3 was a Phase 3, open-label, randomized, multicenter trial that evaluated ABECMA vs standard regimens<sup>†</sup> in 386 patients with RRMM who were triple-class exposed.\* Patients had received 2 to 4 prior regimens including an immunomodulatory agent, a PI, and daratumumab, and were refractory to their last regimen.

In KarMMa-3, ABECMA was studied in patients of varying ages and risk profiles:

- 30 to 81 years of age (median age: 63 years)
- 100% were triple-class exposed
- 95% were daratumumab refractory
- 24% had extramedullary disease
- 28% had high tumor burden
- 42% had high-risk cytogenetics<sup>‡</sup>

**One-time ABECMA infusion in KarMMa-3:** 175 to 529 x 10<sup>6</sup> CAR-positive T cells (n=254)

ABECMA offers unlimited slot availability and the MOST locations near you.<sup>4</sup>

\*Patients who have received an immunomodulatory agent, a PI, and an anti-CD38 monoclonal antibody.<sup>1</sup>

<sup>†</sup>The standard regimens consisted of 5 antimyeloma treatment options: DPd, DVd, IRd, Kd, or EPd, selected by investigator contingent upon the patient's most recent antimyeloma treatment.<sup>1</sup>

<sup>‡</sup>High-risk cytogenetic abnormalities included del(17p), t(4;14), and t(14;16).<sup>3</sup>

DPd=daratumumab, pomalidomide, dexamethasone; DVd=daratumumab, bortezomib, dexamethasone; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EPd=elotuzumab, pomalidomide, dexamethasone; IRd=ixazomib, lenalidomide, dexamethasone; Kd=carfilzomib, dexamethasone; PI=proteasome inhibitor.

### IMPORTANT SAFETY INFORMATION (cont'd)

**Cytokine Release Syndrome (CRS) (cont'd):** Monitor patients at least daily for 7 days following ABECMA infusion for signs or symptoms of CRS. Continue to monitor patients for signs and symptoms of CRS for at least 2 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

**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.

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## Leukapheresis

Collecting your patient's T cells through leukapheresis is the first step in the ABECMA<sup>®</sup> treatment process<sup>1</sup>

**Before leukapheresis begins:**

- Perform screening for CMV, HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing
- Confirm that your patient has been given adequate time after their last anticancer treatment

**Washout periods before leukapheresis in the KarMMa-3 pivotal trial<sup>1,5</sup>**

Systemic MM therapy	Stopped $\geq 14$ days prior to leukapheresis
Corticosteroids (>20 mg/day prednisone or equivalent)*	Stopped $\geq 14$ days prior to leukapheresis

**Following leukapheresis, your patient's T cells are sent to a manufacturing site.<sup>1</sup>**

\*Physiologic replacement, topical, intranasal, and inhaled steroids were permitted in the KarMMa-3 trial.<sup>5</sup> CMV=cytomegalovirus; HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus.

### IMPORTANT SAFETY INFORMATION (cont'd)

**Neurologic Toxicities (cont'd):** 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% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 300 to 460 x 10<sup>6</sup> CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) 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.

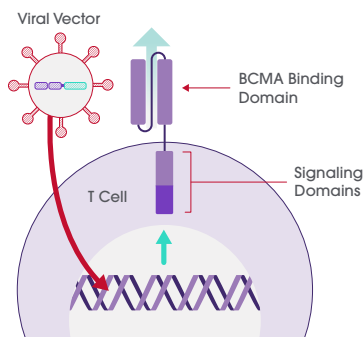
Cerebral edema has been associated with ABECMA in a patient in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have occurred after treatment with ABECMA in another study in multiple myeloma.

**Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).**

## Manufacturing

### At the manufacturing site<sup>1</sup>

- The patient's T cells are transduced with a CAR lentiviral vector targeting BCMA
- The transduced T cells are expanded, formulated into a suspension, and cryopreserved



### Bridging therapy during manufacturing<sup>1,3</sup>

Bridging therapy can be used in some patients at the physician's discretion for disease control during the manufacturing process.

- 85% of patients received bridging therapy in the KarMMa-3 trial

**ABECMA is provided as a single dose for infusion containing a suspension of CAR-positive T cells in 1 or more infusion bags<sup>1</sup>**

- The recommended dose range is 300 to 510 × 10<sup>6</sup> CAR-positive T cells
- ABECMA is an autologous product
- Of 249 patients who underwent leukapheresis, 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

**The median time from leukapheresis to product release was 24 days<sup>6†</sup>**

<sup>†</sup>Based on data reported from January 2024–June 2024.<sup>6</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**Neurologic Toxicities (cont'd):** Monitor patients at least daily for 7 days following ABECMA infusion for signs or symptoms of neurologic toxicities. Continue to monitor patients for signs or symptoms of neurologic toxicities for at least 2 weeks after ABECMA infusion and treat promptly. Rule out other causes of neurologic symptoms. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Counsel patients to seek immediate medical attention should signs or symptoms occur at any time. Advise patients to avoid driving for at least 2 weeks following infusion.

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## Chain of Identity

Pre-infusion

To ensure patient safety, Bristol Myers Squibb requires COI at 4 key points in the treatment process<sup>1,5,7</sup>

Infusion

Post infusion

1. **When you receive the LN<sub>2</sub> dry vapor shipper**  
 Shipper contains RFI certificate and frozen product in LN<sub>2</sub> container. Verify patient identifiers on product RFI certificate match across patient medical records.
2. **After transferring ABECMA<sup>®</sup> to on-site storage\***  
 If on-site vapor phase LN<sub>2</sub> storage is qualified, transfer product container to on-site storage. Verify patient identifiers, including JOIN,<sup>†</sup> match on product RFI certificate and on product labels.
3. **Prior to thawing ABECMA**  
 Verify product containers match product RFI certificate. Verify patient identifiers across all product labels, including JOIN.<sup>†</sup>
4. **Prior to ABECMA administration**  
 Prior to administration, verify patient identifiers match product RFI certificate and patient medical records. Verbally confirm patient identification with patient.

\*Applies to institutions that have demonstrated capacity and have been prequalified for on-site storage.<sup>7</sup>

<sup>†</sup>The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.<sup>7</sup>

COI=chain of identity; LN<sub>2</sub>=liquid nitrogen; RFI=Release for Infusion.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### 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, with a median onset of 6.5 days (range: 4 to 10 days) and occurred in the setting of ongoing or worsening CRS. Five patients with HLH/MAS had overlapping neurotoxicity. 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<sup>6</sup> 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 guidelines.

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## Receiving the ABECMA Shipment

### Cryopreserved ABECMA is shipped to your site in a qualified LN<sub>2</sub> dry vapor shipper<sup>1</sup>

- ABECMA will be shipped on the scheduled date directly to the infusion site's assigned address and/or department, as specified on the Cell Therapy 360<sup>®</sup> Scheduling Portal<sup>7</sup>

#### 1. When you receive the LN<sub>2</sub> dry vapor shipper<sup>7</sup>

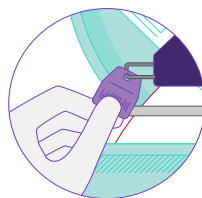
### STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information listed on the RFI certificate matches the information listed on the treatment center's patient medical records:

- Patient's first and last name
- Patient's date of birth
- JOIN<sup>†</sup>

In case of any questions or concerns with the RFI certificate, contact Bristol Myers Squibb at **1-888-805-4555**.

- Confirm the LN<sub>2</sub> dry vapor shipper is free of damage and the tamper-evident tag is intact<sup>1</sup>
  - If the tamper-evident tag is cut or the tag numbers do not match those listed on the shipping label, contact BMS Scheduling by email at [Scheduling@CellTherapy360.com](mailto:Scheduling@CellTherapy360.com) or by phone at 1-888-805-4555 immediately prior to proceeding.



Note the shipper expiration date and time on label inside shipper, and ensure expiration is after the planned date of ABECMA infusion or transfer to on-site storage.<sup>7</sup>

Unless preapproved for on-site storage, do not open the inner container until ready to prepare ABECMA on the day of infusion.<sup>7</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**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.

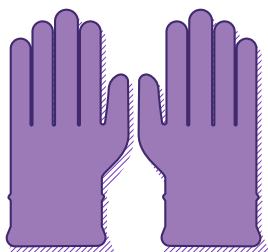
**Infections:** ABECMA should not be administered to patients with active infections or inflammatory disorders. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion.

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## General Guidelines for Safe Handling

Before handling ABECMA<sup>®</sup>, ensure the appropriate safety measures are taken and that personnel have been trained according to institutional practices<sup>7</sup>

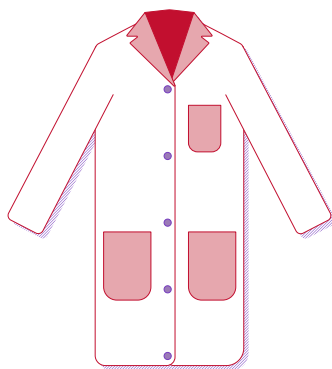
Wear the following personal protective equipment (PPE)



Waterproof thermal protective gloves



Safety glasses with side shields



Lab coat

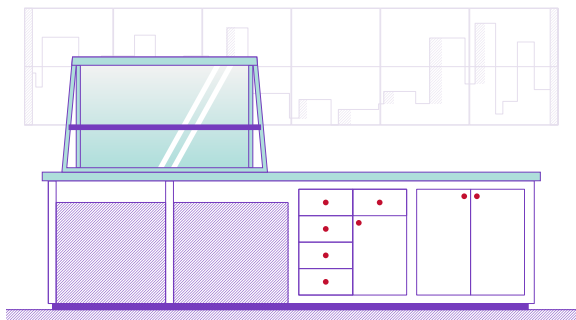
### IMPORTANT SAFETY INFORMATION (cont'd)

**Infections (cont'd):** In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, 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%, viral infections in 7%, 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.

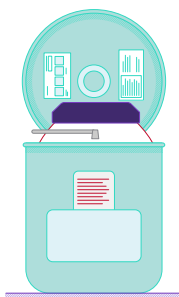
Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

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Always work in a well-ventilated area



Always keep the outer container and LN<sub>2</sub> dry vapor shipper in an upright position<sup>7</sup>



## ABECMA must be handled according to institutional procedures for cellular products, which may contain infectious materials<sup>1</sup>

- 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 to avoid potential transmission of infectious diseases

### IMPORTANT SAFETY INFORMATION (cont'd)

**Infections (cont'd):** 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.

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## LN<sub>2</sub> Dry Vapor Shipper Contents

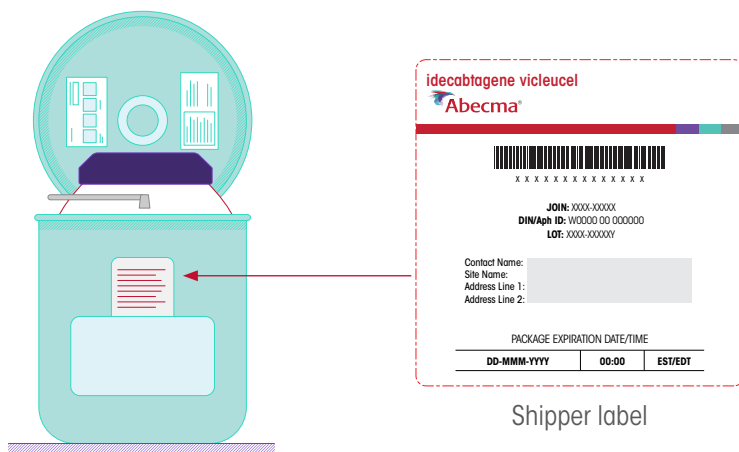
ABECMA<sup>®</sup> is stored within a temperature-controlled LN<sub>2</sub> dry vapor shipper that is placed inside an outer container<sup>1,5</sup>

Affixed to the outside of the outer container are<sup>7</sup>:

- The waybill and shipper receipt documentation
- Return label
- A label containing the shipper expiry and anonymized patient identifiers, including JOIN\*
- Warning labels

Attached to the inside lid of the outer container are<sup>7</sup>:

- The RFI certificate
- ABECMA Prescribing Information and Medication Guide
- A temperature control monitor lies within the outer shipper container and remotely tracks the internal temperature of the LN<sub>2</sub> dry vapor shipper until removal of the drug product



\*The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.<sup>7</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**Prolonged Cytopenias:** 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 89% (123/139) 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<sup>6</sup> CAR-positive T cells and 300 to 460 x 10<sup>6</sup> CAR-positive T cells, respectively.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Inside the LN<sub>2</sub> dry vapor shipper is<sup>1</sup>:

- The ABECMA drug product, which will be packaged in 1 or more infusion bags containing a total of 300 to 510 x 10<sup>6</sup> CAR-positive T cells
  - Each infusion bag is contained within a metal cassette, which is stored in a rack within the LN<sub>2</sub> dry vapor shipper

## ABECMA components<sup>1,5</sup>

- The ABECMA formulation contains Plasma-Lyte A and CryoStor<sup>®</sup> CS10, resulting in a final DMSO concentration of 5%
- ABECMA is cryopreserved and supplied in 1 or more infusion bag(s). The full contents of each infusion bag supplied should be administered
- Each infusion bag is overwrapped with a transparent plastic sleeve that is folded to the back of the overwrap and is contained in a metal cassette. ABECMA is stored in the vapor phase of LN<sub>2</sub> and supplied in an LN<sub>2</sub> dry vapor shipper

The LN<sub>2</sub> dry vapor shipper will be monitored remotely by Bristol Myers Squibb for temperature deviations until the product is received at the site.<sup>7</sup>

**In the event that the temperature goes above -130°C, DO NOT initiate ABECMA infusion, and call Bristol Myers Squibb at 1-888-805-4555 to determine next steps.<sup>7</sup>**

DMSO=dimethyl sulfoxide.

## IMPORTANT SAFETY INFORMATION (cont'd)

**Prolonged Cytopenias (cont'd):** Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines.

**Hypogammaglobulinemia:** In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, hypogammaglobulinemia was reported as an adverse event in 13% (46/349) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 37% (130/349) of patients treated with ABECMA.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 45% (158/349) of patients treated with ABECMA. Forty-one percent of patients received intravenous immunoglobulin (IVIG) post-ABECMA for serum IgG <400 mg/dL.

Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dL. Manage appropriately per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

**Use of Live Vaccines:** The safety of immunization with live viral vaccines during or after ABECMA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during ABECMA treatment, and until immune recovery following treatment with ABECMA.

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## ABECMA<sup>®</sup> Storage

### The method of storage will depend on individual site capabilities<sup>7</sup>

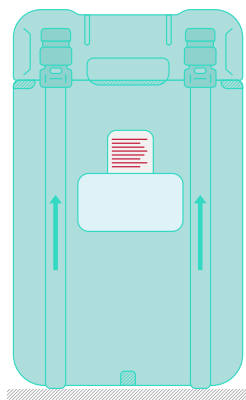
There are 2 delivery/storage options for ABECMA:

#### Method 1: Just-in-time delivery

ABECMA arrives on or near the date of infusion and remains in the LN<sub>2</sub> dry vapor shipper until the product is thawed for patient administration.

**NOTE: The LN<sub>2</sub> dry vapor shipper will arrive the day of intended infusion or earlier, pending delivery logistics and agreement with the infusion site.**

- The LN<sub>2</sub> dry vapor shipper should be stored upright in a LOCKED, WELL-VENTILATED room upon arrival at the site and until time of infusion of ABECMA
- If ABECMA is received earlier than the intended infusion day, it can be kept temporarily in the LN<sub>2</sub> dry vapor shipper until the time of infusion, as long as it does not exceed the maximum allowable LN<sub>2</sub> dry vapor shipper storage duration
- Storage of the LN<sub>2</sub> dry vapor shipper should not exceed the shipper expiration date; planned date of administration should be before this expiration date for just-in-time delivery
- 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 on-site storage, contact Bristol Myers Squibb at 1-888-805-4555 to arrange for return shipment



### IMPORTANT SAFETY INFORMATION (cont'd)

**Secondary Malignancies:** Patients treated with ABECMA may develop secondary malignancies. In KarMMa-3, myeloid neoplasms (four cases of myelodysplastic syndrome and one case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the standard regimens arm at the time of the safety update. The median time to onset of myeloid neoplasm from ide-cel infusion was 338 days (Range: 277 to 794 days). Three of these five patients have died following the development of myeloid neoplasm. One out of the five cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Method 2: On-site storage (by preapproval process)<sup>7\*</sup>

ABECMA is transferred to on-site vapor-phase LN<sub>2</sub> storage.

- Preparation for transfer
  - The transfer should be completed by 2 qualified site staff who can ensure it is done within 2 minutes
  - Prepare for the upcoming COI checks by locating the RFI certificate and identifying the location of the data points required for COI check #2
- On-site institutional temperature monitoring: Store ABECMA frozen in the vapor phase of LN<sub>2</sub> (-130°C or colder)
  - In the event that the temperature goes above -130°C, **DO NOT** initiate ABECMA infusion, and call Bristol Myers Squibb at 1-888-805-4555
- Upon arrival, ABECMA should be transferred to on-site vapor-phase LN<sub>2</sub> storage. Complete the transfer to on-site storage within 2 minutes
  - Remove the metal cassettes within the LN<sub>2</sub> dry vapor shipper
  - Transfer the metal cassettes to your site's storage rack immediately
  - During transfer, keep the metal cassette over the vapor phase of the shipper to prevent thawing
  - Complete COI check #2 outlined in the purple box below

### 2. After transferring ABECMA to on-site storage<sup>7</sup>

## STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information listed on the product RFI certificate matches the information listed on the cassette labels<sup>†</sup>:

- Patient's first and last name
- Patient's date of birth
- JOIN<sup>‡</sup>

**NOTE:** This COI check only occurs if storing ABECMA in on-site vapor-phase LN<sub>2</sub> storage.

\*Applies to institutions that have demonstrated capacity and have been prequalified for on-site storage.<sup>7</sup>

<sup>†</sup>ABECMA infusion bags will arrive in a labeled cassette.<sup>7</sup>

<sup>‡</sup>The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.<sup>7</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**Secondary Malignancies (cont'd):** T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes.

Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Lymphodepleting Chemotherapy

### Begin administration of low-dose lymphodepleting chemotherapy 5 days before ABECMA<sup>®</sup> infusion<sup>1</sup>

- ✓ Confirm the availability of ABECMA before starting the lymphodepleting chemotherapy regimen
- ✓ Administer lymphodepleting chemotherapy regimen: fludarabine 30 mg/m<sup>2</sup>/day IV and cyclophosphamide 300 mg/m<sup>2</sup>/day IV for 3 days\*
- ✓ Administer ABECMA 2 days after completion of lymphodepleting chemotherapy

Delay the infusion of ABECMA for 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 the Prescribing Information of cyclophosphamide and fludarabine for information on dose adjustment in renal impairment.<sup>1</sup>

IV=intravenous.

### IMPORTANT SAFETY INFORMATION (cont'd)

**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.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

# Considerations Before Lymphodepleting Chemotherapy



## Washout periods before lymphodepleting chemotherapy in the KarMMa-3 trial<sup>1</sup>

MM bridging therapies  
(following leukapheresis)

Stopped  $\geq 14$  days prior to  
lymphodepleting chemotherapy

- Some patients may have an urgent need for treatment, and you may not consider them candidates for ABECMA
- However, an effective bridging therapy can be administered to maintain disease control during the ABECMA manufacturing process
  - This may make ABECMA accessible to more patients

### IMPORTANT SAFETY INFORMATION

#### Warnings and Precautions:

**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%). 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.

**Cytokine Release Syndrome (CRS):** CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including  $\geq$  Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) 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 63 days). In the pooled studies, the rate of  $\geq$ Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10<sup>6</sup> CAR-positive T cells.

The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Preparing for the Infusion

### Before beginning treatment with ABECMA<sup>®1</sup>

- ✓ Ensure that a minimum of 2 doses of tocilizumab per patient and emergency equipment are available prior to infusion and during the recovery period
- ✓ Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. ABECMA should not be administered to patients with active infections or inflammatory disorders
- ✓ Monitor complete blood counts prior to and after ABECMA infusion

ABECMA may cause a false-positive HIV test result by some commercial tests.

### Premedication on infusion day<sup>1</sup>

30–60 minutes before ABECMA infusion:

- ✓ Administer acetaminophen (650 mg orally) and diphenhydramine (12.5 mg IV or 25 to 50 mg orally, or another H<sub>1</sub>-antihistamine)

Avoid prophylactic use of dexamethasone or other systemic corticosteroids, as they may interfere with the activity of ABECMA.<sup>1</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**Cytokine Release Syndrome (CRS) (cont'd):** 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 10<sup>6</sup> CAR-positive T cells, 76% (54/71) of patients received 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 10<sup>6</sup> 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.

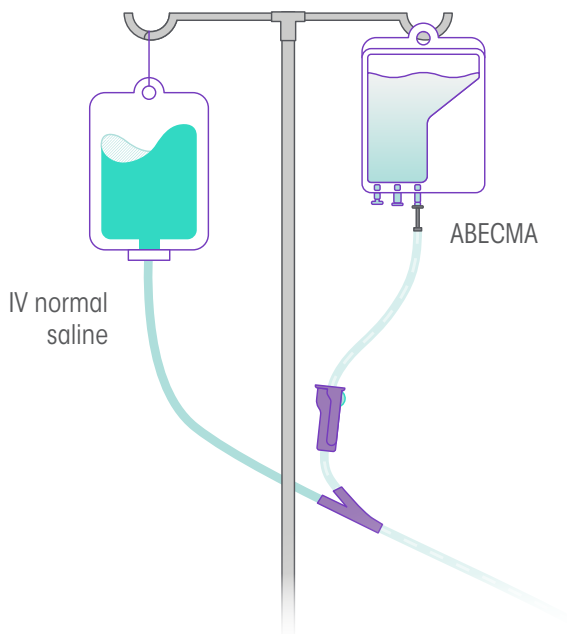
Monitor patients at least daily for 7 days following ABECMA infusion for signs or symptoms of CRS. Continue to monitor patients for signs and symptoms of CRS for at least 2 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Setup<sup>7</sup>

A Y-type administration set is recommended to accommodate the infusion bag on 1 arm and a bag of normal saline on the second arm.

- ABECMA can be administered via peripheral or central venous access. Central venous access is encouraged in patients with poor peripheral access



DO NOT use a leukodepleting filter.<sup>7</sup>

## IMPORTANT SAFETY INFORMATION (cont'd)

**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% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 300 to 460 x 10<sup>6</sup> CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Preparing to Thaw ABECMA<sup>®</sup>

### Ensure that the following steps are completed prior to thawing ABECMA<sup>7</sup>:

When removing ABECMA from vapor-phase LN<sub>2</sub> storage, proper PPE should be worn. Ensure that personnel are trained on the handling of LN<sub>2</sub> according to institutional practices.

- ✓ Have the RFI certificate ready
- ✓ Confirm with site staff that the patient is ready for infusion and has been appropriately premedicated
- ✓ Confirm the infusion start time in advance and adjust the start time of the thaw so that ABECMA is available for infusion when the patient is ready
- ✓ Preheat approved thaw device or water bath to 37°C
- ✓ Verify that the number of infusion bags and label information match the ABECMA RFI certificate

### IMPORTANT SAFETY INFORMATION (cont'd)

**Neurologic Toxicities (cont'd):** 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 for signs or symptoms of neurologic toxicities. Continue to monitor patients for signs or symptoms of neurologic toxicities for at least 2 weeks after ABECMA infusion and treat promptly. Rule out other causes of neurologic symptoms. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Counsel patients to seek immediate medical attention should signs or symptoms occur at any time. Advise patients to avoid driving for at least 2 weeks following infusion.

#### **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, with a median onset of 6.5 days (range: 4 to 10 days) and occurred in the setting of ongoing or worsening CRS. Five patients with HLH/MAS had overlapping neurotoxicity. 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<sup>6</sup> 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.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

### 3. Prior to thawing ABECMA<sup>7</sup>

## STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information on the ABECMA RFI certificate matches the cassette labels and bag labels:

- Patient's first and last name
- Patient's date of birth
- JOIN\*

**NOTE:** Do not remove the ABECMA infusion bag from the cassette if the information on the patient-specific label 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.

\*The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.<sup>7</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

#### Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS) (cont'd):

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 guidelines.

**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.

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

In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, 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%, viral infections in 7%, 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.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

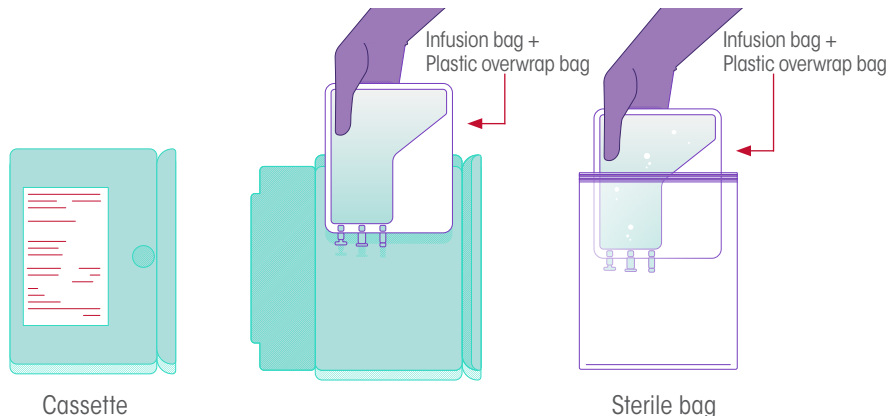
## ABECMA<sup>®</sup> Thawing

NOTE: The ABECMA infusion bags should be administered in series. If more than 1 infusion bag is required for administration, **keep the remaining bag(s) in LN<sub>2</sub> storage until prior bag has been infused and patient is ready; proceed to the subsequent infusion bag based on clinical judgment.** Each infusion bag must be administered within 1 hour of the thaw process.<sup>1\*</sup>

### Step 1<sup>7</sup>

Open the cassette for the first infusion bag, gently remove from cassette, and immediately place the infusion bag inside a second sterile bag without removing the protective overwrap plastic bag per local guidelines.

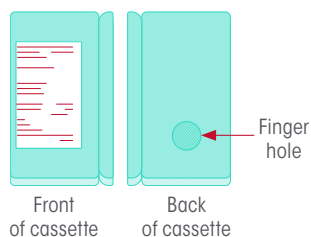
- **DO NOT** unfold the label flap
- Inspect the infusion bag for any breaches of integrity such as breaks or cracks before thawing. If the bag is compromised, contact Bristol Myers Squibb at 1-888-805-4555
- Recommend recording the start time of the thaw and expiry for the thaw bag on the ABECMA RFI certificate or product label. Thaw begins when the infusion bag is removed from LN<sub>2</sub> storage



NOTE: Cassette appearance may differ depending on infusion bag size (50 mL, 250 mL, or 500 mL).<sup>1</sup>

### Tips specific for removing the 50 mL infusion bag from the cassette

- Hold open cassette in one hand
- With the opposite hand, use one finger to gently push bag from the back of the cassette to pop up the bag



\*ABECMA is stable for 2 hours at room temperature once thawed.<sup>1</sup>

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

- Additionally, while not recommended for retrieving materials from within the LN<sub>2</sub> dry vapor shipper or extended exposure to cryogenic temperatures, rubber-coated cryogenic gloves may provide better dexterity for removing the bag from the cassette

## Step 2<sup>7</sup>

Thaw ABECMA at approximately 37°C using an approved thaw device or water bath until there is no visible ice in the infusion bag.

- Gently mix the contents of the bag to disperse visible clumps of cellular material. Small clumps of cellular material may persist despite gentle manual mixing
- **DO NOT** walk away from the thawing product
- **DO NOT** wash, spin down, and/or resuspend ABECMA in new media prior to infusion

If more than 1 infusion bag has been received for treatment, thaw each infusion bag 1 at a time.

## Step 3<sup>7</sup>

If thawing in a cell therapy lab, transport ABECMA to bedside in an insulated room temperature carrier. Note: thaw begins at time ABECMA is removed from frozen storage. After thawing, gently remove the infusion bag from the overwrap by unfolding the plastic sleeve at the back to expose the infusion bag. Gently pull the infusion bag out of the overwrap.

Provide the RFI certificate to the staff performing product administration.

## Repeat<sup>7</sup>

Follow the same procedure for all subsequent infusion bags for the identified patient.

### IMPORTANT SAFETY INFORMATION (cont'd)

**Infections (cont'd):** *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.

**Prolonged Cytopenias:** 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 89% (123/139) 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<sup>6</sup> CAR-positive T cells and 300 to 460 x 10<sup>6</sup> CAR-positive T cells, respectively.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## ABECMA<sup>®</sup> Infusion Process

After obtaining the RFI certificate, ensure that the following steps are completed immediately before administering ABECMA<sup>1,5,7</sup>:

- ✔ Conduct a general nursing assessment
- ✔ Check for fever or infection, monitor complete blood counts, and confirm the patient can appropriately receive ABECMA
- ✔ Confirm that the patient has been appropriately premedicated
- ✔ Determine peripheral or central venous access
- ✔ Confirm 1 hour after thaw has not passed
- ✔ Prime the tubing of the infusion set with normal saline prior to infusion. An infusion set with an in-line filter (non-leukodepleting filter with a pore size range of 170 to 260  $\mu\text{m}$ ) can be used for thawed products with visible clumps of cellular material that do not disperse after gentle manual mixing
- ✔ Gently massage the thawed infusion bag and attach it to the administration set

NOTE: The ABECMA infusion bags should be administered in series. If more than 1 infusion bag is required for administration, **keep the remaining bag(s) in LN<sub>2</sub> storage until prior bag has been infused and patient is ready; proceed to the subsequent infusion bag based on clinical judgment.** Each infusion bag should be infused within 1 hour of the start of its thaw.\*

\*ABECMA is stable for 2 hours at room temperature once thawed.<sup>1</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

**Prolonged Cytopenias (cont'd):** Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines.

**Hypogammaglobulinemia:** In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, hypogammaglobulinemia was reported as an adverse event in 13% (46/349) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 37% (130/349) of patients treated with ABECMA.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 45% (158/349) of patients treated with ABECMA. Forty-one percent of patients received intravenous immunoglobulin (IVIG) post-ABECMA for serum IgG <400 mg/dL.

Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dL. Manage appropriately per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

#### 4. Prior to ABECMA administration<sup>7</sup>

## STOP AND CONFIRM PATIENT ID

Two site staff are required to verify the patient information on the ABECMA RFI certificate matches the cassette labels and bag labels:

- Patient's first and last name
- Patient's date of birth
- JOIN<sup>†</sup>

Site staff must verify patient information on product labels against the patient's medical records, as well as verbally with the patient prior to infusion.

**Each infusion bag should be infused within 1 hour from start of thaw<sup>1</sup>**

### Step 1

Infuse the contents of the infusion bag by gravity flow.

### Step 2

After the entire content of the infusion bag is infused, rinse the tubing, inclusive of the in-line filter if used, with 30 mL to 60 mL of normal saline at the same infusion rate to ensure as many cells as possible are infused into the patient.

### Step 3

If more than 1 infusion bag is administered, administer all bags as directed, and repeat the procedure (thawing through saline flush). Do not initiate thaw of the next bag until infusion of the previous bag is complete.

<sup>†</sup>The JOIN is a unique identification code that is assigned to the patient's specific cellular material and is the link between the patient and their cells throughout the manufacturing process.<sup>7</sup>

## IMPORTANT SAFETY INFORMATION (cont'd)

**Hypogammaglobulinemia (cont'd):** Use of Live Vaccines: The safety of immunization with live viral vaccines during or after ABECMA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during ABECMA treatment, and until immune recovery following treatment with ABECMA.

**Secondary Malignancies:** Patients treated with ABECMA may develop secondary malignancies. In KarMMa-3, myeloid neoplasms (four cases of myelodysplastic syndrome and one case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the standard regimens arm at the time of the safety update. The median time to onset of myeloid neoplasm from ide-cel infusion was 338 days (Range: 277 to 794 days). Three of these five patients have died following the development of myeloid neoplasm. One out of the five cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy.

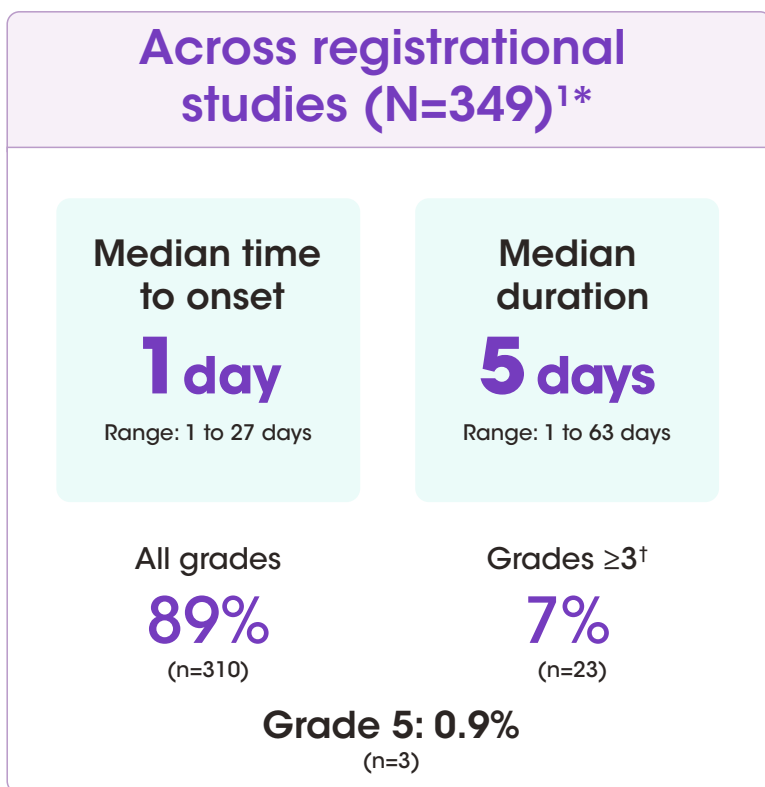
Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Cytokine Release Syndrome

During administration and at least daily for the first 7 days following ABECMA<sup>®</sup> infusion, monitor your patients for adverse reactions<sup>1</sup>

These reactions can include CRS and neurologic toxicity:

- Refer to the CRS and neurologic toxicity tables on pages 28–29 and 32–33 for grading and management
- Accurate grading is imperative for appropriate management



CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA.

\*Pooled registrational studies included KarMMa-3 and KarMMa (5L+).

<sup>†</sup>Lee criteria for grading CRS (Lee et al, 2014).

5L=fifth-line.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Monitoring and management of CRS<sup>1</sup>

- **Counsel** patients to seek immediate medical attention should signs or symptoms of CRS occur at any time
  - Symptoms of CRS include fever, difficulty breathing, dizziness or light-headedness, nausea, headache, fast heartbeat, low blood pressure, or fatigue
- **Instruct** patients to remain within proximity of a healthcare facility for at least 2 weeks following infusion
- **Monitor** patients for signs and symptoms of CRS
  - At least daily for 7 days following ABECMA infusion
  - For at least 2 weeks after ABECMA infusion
- **Treat** at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as needed based on the grading and management guidelines
  - If CRS is suspected, manage according to the recommendations in the full Prescribing Information
  - If concurrent neurologic toxicity is suspected during CRS, manage CRS according to the recommendations in the full Prescribing Information
- **Ensure** that a minimum of 2 doses of tocilizumab per patient are available prior to infusion of ABECMA

## CRS Treatment<sup>1</sup>

- Treat at the first sign of CRS with supportive care, tocilizumab, and/or corticosteroids as indicated
- Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension
- CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap
  - In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS
  - 65% (226/349) of patients received tocilizumab
  - 39% (135/349) received a single dose
  - 26% (91/349) received more than 1 dose
- 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

**If CRS is suspected, manage according to the recommendations in the tables on pages [28-29](#).**

HLH/MAS=hemophagocytic lymphohistiocytosis/macrophage activation syndrome.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Cytokine Release Syndrome (cont'd)

### CRS grading from the ABECMA<sup>®</sup> Prescribing Information<sup>1\*</sup>

<b>Grade 1</b>	Symptoms require symptomatic treatment only (eg, fever, nausea, fatigue, headache, myalgia, malaise).
<b>Grade 2</b>	Symptoms require and respond to moderate intervention. Oxygen requirement <40% FiO <sub>2</sub> or hypotension responsive to fluids, or low dose of 1 vasopressor, or Grade 2 organ toxicity.
<b>Grade 3</b>	Symptoms require and respond to aggressive intervention. Fever, oxygen requirement ≥40% FiO <sub>2</sub> , or hypotension requiring high-dose or multiple vasopressors, or Grade 3 organ toxicity or Grade 4 transaminitis.
<b>Grade 4</b>	Life-threatening symptoms. Requirements for ventilator support, continuous veno-venous hemodialysis (CVVHD), or Grade 4 organ toxicity (excluding transaminitis).



The ASTCT Consensus Grading system is another guideline for evaluating cell therapy-associated CRS. Please refer to these guidelines for additional information.<sup>5</sup>

ASTCT=American Society for Transplantation and Cellular Therapy; CVVHD=continuous venovenous hemodialysis.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## CRS management guidance from the ABECMA Prescribing Information<sup>1\*</sup>

Tocilizumab <sup>†</sup>	Corticosteroids <sup>‡</sup>
<b>Grade 1</b>	
<p>If onset ≥72 hours after infusion, treat symptomatically.</p> <p>If onset &lt;72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).</p>	<p>Consider dexamethasone 10 mg IV every 24 hours.</p>
<b>Grade 2</b>	
<p>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).</p> <p>Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.</p> <p>Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</p>	<p>Consider dexamethasone 10 mg IV every 12–24 hours.</p>
<p>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).</p> <p>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 anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</p>	
<b>Grade 3</b>	
<p>Per Grade 2.</p>	<p>Administer dexamethasone 10 mg IV every 12 hours.</p>
<p>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).</p> <p>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 anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</p>	
<b>Grade 4</b>	
<p>Per Grade 2.</p>	<p>Administer dexamethasone 20 mg IV every 6 hours.</p>
<p>After 2 doses of tocilizumab, consider alternative anticytokine agents. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</p> <p>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.</p>	

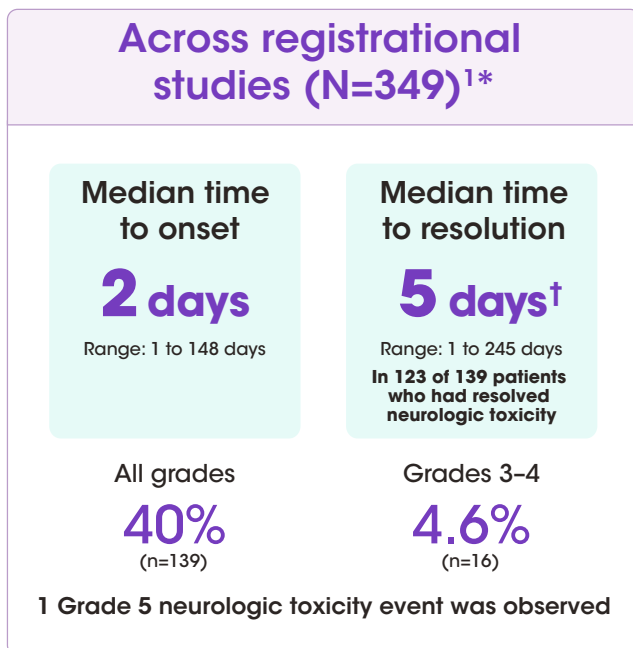
<sup>1</sup>Lee criteria for grading CRS (Lee et al 2014).

<sup>†</sup>Refer to tocilizumab Prescribing Information for details.

<sup>‡</sup>If corticosteroids are initiated, continue corticosteroids for at least 3 doses, and taper over a maximum of 7 days.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Neurologic Toxicity



- Cerebral edema has been associated with ABECMA<sup>®</sup> in a patient in another study in multiple myeloma<sup>1</sup>
- Neurologic toxicities, which may be severe or life-threatening, including immune-effector cell-associated neurotoxicity (ICANS), occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS<sup>1</sup>

No cases of parkinsonism or Guillain-Barré syndrome were observed across registrational studies<sup>8\*†</sup>

Through March 2024,<sup>§</sup> postmarketing reporting in the BMS safety database notes that out of the 3167 cases seen with ABECMA, there were<sup>8§</sup>:

- 5 cases of parkinsonism (0.16%)<sup>||</sup>
- 0 cases of Guillain-Barré syndrome<sup>¶</sup>

<sup>8</sup>Two of the 5 cases reported in the postmarketing BMS safety database had fatal outcomes due to any cause.<sup>8</sup> One fatal case reported after March data update and remains under investigation.

<sup>†</sup>One fatal case reported after March data update and remains under investigation.<sup>8</sup>

\*Pooled registrational studies included KarMMa-3 and KarMMa (5L+).<sup>1</sup>

<sup>1</sup>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 cutoff.<sup>1</sup>

<sup>2</sup>Grade 3 myelitis and grade 3 parkinsonism have occurred after treatment with ABECMA in another study in multiple myeloma. National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) criteria (version 4.03) utilized for grading neurologic toxicities.<sup>1</sup>

<sup>§</sup>Additional cases, including fatal cases, may be reported and be under investigation after the data cutoff. These cases will be included at the next safety update. Identification and addition of adverse events into the BMS postmarketing safety database is dependent on physician reporting and grading perspectives. Postmarketing surveillance is voluntary and adverse events may potentially be under-reported.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Monitoring and management of neurologic toxicity<sup>1</sup>

- **Counsel** patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time
- **Instruct** patients to remain within proximity of a healthcare facility center for at least 2 weeks following infusion
- **Monitor** patients for signs and symptoms of neurologic toxicity
  - At least daily for 7 days following ABECMA infusion
  - For at least 2 weeks after ABECMA infusion
- **Exclude** other causes of neurologic signs or symptoms
- **Treat** promptly with supportive care and/or corticosteroids as needed based on the grading and management guidelines
  - If neurologic toxicity is suspected, manage according to the recommendations in the full Prescribing Information
  - If concurrent CRS is suspected during the neurologic toxicity event, manage CRS according to the recommendations in the full Prescribing Information
  - Patients with any-grade neurologic toxicity should be treated with non-sedating antiseizure medicine for seizure prophylaxis

If neurologic toxicity is suspected, manage according to the recommendations in the table on pages [32–33](#).

Management recommendations from the Prescribing Information for each grade of CRS and neurologic toxicity are outlined in the tables on pages [28–29](#) and [32–33](#), respectively.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Neurologic Toxicity (cont'd)

### Neurologic toxicity management guidance from the ABECMA<sup>®</sup> Prescribing Information<sup>1</sup>

Grade*	Corticosteroids and antiseizure medicines
<b>Grade 1</b>	<p>Start nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>If ≥72 hours after infusion, observe patient.</p> <p>If &lt;72 hours after infusion, consider dexamethasone 10 mg IV every 12 to 24 hours for 2 to 3 days.</p>
<b>Grade 2</b>	<p>Start nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 10 mg IV every 12 hours for 2 to 3 days, or longer for persistent symptoms.</p> <p>Consider taper for a total steroid exposure of &gt;3 days. Corticosteroids are not recommended for isolated Grade 2 headaches.</p> <p>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.</p>

Pre-infusion

Infusion

Post infusion

\*NCI CTCAE criteria was used for grading neurologic toxicities.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

**Grade\*****Corticosteroids and antiseizure medicines**

<b>Grade 3</b>	<p>Start nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 10 to 20 mg IV every 6 to 12 hours. Corticosteroids are not recommended for isolated Grade 3 headaches.</p> <p>If no improvement after 24 hours or worsening of neurologic toxicity, escalate to methylprednisolone (2 mg/kg loading dose, followed by 2 mg/kg divided into 4 times a day; taper within 7 days).</p> <p>If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1–2 g, repeat every 24 hours if needed; taper as clinically indicated) and cyclophosphamide 1.5 g/m<sup>2</sup>.</p>
<b>Grade 4</b>	<p>Start nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.</p> <p>Start dexamethasone 20 mg IV every 6 hours.</p> <p>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).</p> <p>If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylprednisolone (1–2 g, repeat every 24 hours if needed; taper as clinically indicated), and cyclophosphamide 1.5 g/m<sup>2</sup>.</p>

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## ARs of Significance

### HLH/MAS<sup>1</sup>

#### In KarMMa-3 (N=222):

- One patient had Grade 5, 2 patients had grade 4, and 2 patients had Grade 3 HLH/MAS
- Two cases of grade 3 and 1 case of Grade 4 HLH/MAS had resolved

#### In KarMMa (N=127):

- One patient treated in the 300 x 10<sup>6</sup> 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

#### Across registrational studies (N=349)\*:

- HLH/MAS occurred in 2.9% (10/349) of patients
- All events of HLH/MAS had onset within 10 days of receiving ABECMA<sup>®</sup> and occurred in the setting of ongoing or worsening CRS
- Median time to onset was 6.5 days (range: 4 to 10 days)
- Five patients had overlapping neurotoxicity

### Prolonged cytopenias<sup>1</sup>

#### Across registrational studies (N=349)\*:

- Prolonged neutropenia rates: 40% Grade ≥3 (n=139)
  - Median time to recovery was 1.9 months in 89% (n=123/139) of patients who recovered from Grade 3 or 4 neutropenia after month 1
- Prolonged thrombocytopenia rates: 42% Grade ≥3 (n=145)
  - Median time to recovery was 1.9 months in 76% (n=110/145) of patients who recovered from Grade 3 or 4 thrombocytopenia

### Early death<sup>1</sup>

- 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 with the standard regimen arm (15/132; 11%)

\*Pooled registrational studies included KarMMa-3 and KarMMa (5L+).

AR=adverse reaction.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

- Early deaths occurred in 8% (20/254) and 0% of patients 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
- 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. 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

Before selecting ABECMA, please consider the elements of KarMMa-3 trial design, such as patient inclusion criteria and treatment approach.

### Secondary Malignancies<sup>1</sup>

- In KarMMa-3, myeloid neoplasms (4 cases of myelodysplastic syndrome and 1 case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared with none in the control arm at the time of the safety update
- Median time to onset of myeloid neoplasm from ABECMA infusion was 338 days (range: 277 to 794 days); 3 out of 5 of these patients died following the development of myeloid neoplasm

T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Monitor life-long for secondary malignancies.

## ABECMA Safety Profile

### Most common adverse reactions<sup>1</sup>

- The most common nonlaboratory adverse reactions (incidence  $\geq 20\%$ ) included 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
- The most common Grade 3 or 4 laboratory adverse reactions (incidence  $\geq 50\%$ ) included leukocyte count decreased, neutrophil count decreased, lymphocyte count decreased, platelet count decreased, and hemoglobin decreased

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## ABECMA<sup>®</sup> Safety Profile (cont'd)

Adverse reactions observed in at least 10% of patients treated with ABECMA in the KarMMa-3 study (N=222)<sup>1</sup>

	Any Grade (%)	Grade 3 or Higher (%)
<b>Blood and lymphatic system disorders</b>		
Febrile neutropenia	51	51
Coagulopathy <sup>a</sup>	14	2.7
<b>Cardiac disorders</b>		
Tachycardia <sup>b</sup>	32	0
<b>Gastrointestinal disorders</b>		
Diarrhea <sup>c</sup>	31	2.3
Nausea	27	0.9
Constipation	17	0
Vomiting <sup>d</sup>	14	0
Abdominal pain <sup>e</sup>	10	0.5
<b>General disorders and administration site conditions</b>		
Pyrexia	91	9
Fatigue <sup>f</sup>	33	1.4
Edema <sup>g</sup>	20	0.5
Chills	19	0.5

<sup>a</sup>Coagulopathy includes activated partial thromboplastin time prolonged, blood fibrinogen decreased, coagulopathy, disseminated intravascular coagulation, hypofibrinogenemia, international normalized ratio increased, prothrombin time prolonged.

<sup>b</sup>Tachycardia includes heart rate increased, sinus tachycardia, tachycardia.

<sup>c</sup>Diarrhea includes colitis, colitis microscopic, diarrhea, enterocolitis.

<sup>d</sup>Vomiting includes retching, vomiting.

<sup>e</sup>Abdominal pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, dyspepsia.

<sup>f</sup>Fatigue includes asthenia, fatigue, malaise, muscle fatigue.

<sup>g</sup>Edema includes edema, edema peripheral, generalized edema, peripheral swelling, swelling, eyelid edema, face edema, fluid retention, hypervolemia, localized edema, mouth swelling, periorbital edema, periorbital swelling, swelling face.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

Pre-infusion

Infusion

Post infusion

	Any Grade (%)	Grade 3 or Higher (%)
<b>Immune system disorders</b>		
Cytokine release syndrome	91	4.1
Hypogammaglobulinemia	48	0.9
<b>Infections and infestations</b>		
Any Infection	56	16
Infections—Pathogen unspecified <sup>h</sup>	35	9
Upper respiratory tract infection <sup>i</sup>	19	1.8
Infections—Viral <sup>h</sup>	18	5
Infections—Bacterial <sup>h</sup>	15	4.5
Pneumonia <sup>j</sup>	13	8
<b>Metabolism and nutrition disorders</b>		
Decreased appetite	17	1.8
<b>Musculoskeletal and connective tissue disorders</b>		
Musculoskeletal pain <sup>k</sup>	36	1.8
<b>Nervous system disorders</b>		
Headache <sup>l</sup>	24	0
Encephalopathy <sup>m</sup>	22	3.6
Dizziness <sup>n</sup>	14	1.8
Neuropathy <sup>o</sup>	10	0

<sup>h</sup>Infections and infestations System Organ Class Adverse Events are grouped by high level grouped term (HLGT) pathogen type.

<sup>i</sup>Upper respiratory tract infection includes acute sinusitis, epiglottitis, HCoV-OC43 infection, nasopharyngitis, pharyngeal inflammation, pharyngitis, pharyngitis streptococcal, respiratory tract infection, respiratory tract infection bacterial, rhinitis, rhinovirus infection, sinusitis, upper respiratory tract infection, viral upper respiratory tract infection.

<sup>j</sup>Pneumonia includes bronchopulmonary aspergillosis, coronavirus pneumonia, COVID-19 pneumonia, organizing pneumonia, pneumonia, pneumonia acinetobacter, pneumonia adenoviral, pneumonia aspiration, pneumonia bacterial, pneumonia fungal, pneumonia influenza, pneumonia legionella, pneumonia parainfluenza viral, pneumonia pseudomonal, pneumonia streptococcal, pneumonia viral, pulmonary nocardiosis.

<sup>k</sup>Musculoskeletal pain includes arthralgia, back pain, bone pain, joint stiffness, muscle strain, musculoskeletal chest pain, musculoskeletal discomfort, musculoskeletal pain, musculoskeletal stiffness, myalgia, neck pain, non-cardiac chest pain.

<sup>l</sup>Headache includes headache, head discomfort.

<sup>m</sup>Encephalopathy includes amnesia, cognitive disorder, confusional state, depressed level of consciousness, disturbance in attention, dysgraphia, encephalopathy, immune effector cell-associated neurotoxicity syndrome incoherent, lethargy, memory impairment, mental status changes, metabolic encephalopathy, somnolence, stupor, toxic encephalopathy.

<sup>n</sup>Dizziness includes dizziness, presyncope, syncope, vertigo, vertigo positional, vestibular disorder.

<sup>o</sup>Neuropathy includes carpal tunnel syndrome, dysesthesia, hyperesthesia, hypoesthesia, hypoesthesia oral, mononeuropathy, neuralgia, neuritis, neuropathy peripheral, paresthesia, paresthesia oral, peripheral motor neuropathy, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, peroneal nerve palsy, radicular pain, radiculopathy, sacral radiculopathy, sciatica, sensory loss, toxic neuropathy.

**Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and **Medication Guide**.**

Pre-infusion

Infusion

Post infusion

## ABECMA<sup>®</sup> Safety Profile (cont'd)

Adverse reactions observed in at least 10% of patients treated with ABECMA in the KarMMa-3 study (N=222)<sup>1</sup>

	Any Grade (%)	Grade 3 or Higher (%)
<b>Psychiatric disorders</b>		
Sleep disorder <sup>p</sup>	11	0
<b>Renal and urinary disorders</b>		
Renal failure <sup>q</sup>	13	5
<b>Respiratory, thoracic, and mediastinal disorders</b>		
Dyspnea <sup>r</sup>	21	1.8
Cough <sup>s</sup>	14	0
Hypoxia <sup>t</sup>	18	6
<b>Vascular disorders</b>		
Hypotension <sup>u</sup>	36	2.3
Hypertension	14	7
<b>Skin Disorders</b>		
Rash <sup>v</sup>	10	0

<sup>p</sup>Sleep disorder includes hypersomnia, insomnia, sleep disorder.

<sup>q</sup>Renal failure includes acute kidney injury, blood creatinine increased, chronic kidney disease, creatinine renal clearance decreased, glomerular filtration rate decreased, nephropathy toxic, oliguria, renal failure, renal impairment, urine output decreased.

<sup>r</sup>Dyspnea includes dyspnea, dyspnea exertional, dyspnea paroxysmal nocturnal, tachypnea.

<sup>s</sup>Cough includes cough, productive cough, upper-airway cough syndrome.

<sup>t</sup>Hypoxia includes hypoxia, oxygen saturation decreased.

<sup>u</sup>Hypotension includes hemodynamic instability, hypotension, orthostatic hypotension.

<sup>v</sup>Rash includes acne, catheter site dermatitis, catheter site rash, dermatitis, dermatitis contact, drug eruption, eczema, erythema, papulopustular rosacea, photosensitivity reaction, rash, rash follicular, rash macular, rash maculo-papular, rash papular, rash pruritic, skin irritation, skin lesion, urticaria.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Grade 3 or 4 laboratory abnormalities worsening from baseline in $\geq 10\%$ of patients treated with ABECMA in the KarMMa-3 study<sup>1</sup>

	175-529 x 10 <sup>6</sup> CAR-Positive T Cells (N=222)
	Grade 3 or 4 (%)
Lymphocyte decreased	98
Leukocyte decreased	96
Neutrophil decreased	96
Platelet decreased	59
Hemoglobin decreased	52
Phosphate decreased	45
Triglyceride increased	21
Alanine aminotransferase increased	13
Sodium decreased	11
Gamma-glutamyltransferase increased	10

Laboratory tests were graded according to NCI CTCAE Version 4.03. Laboratory abnormalities are sorted by decreasing frequency.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Returning the LN<sub>2</sub> Dry Vapor Shipper<sup>7</sup>

1. Load the cassette rack into the inner chamber of the outer container and replace the inner chamber lid
2. Remove shipping pouch from the pocket inside the outer container. The shipping pouch contains the return label and an "EMPTY" label
3. Remove the "EMPTY" label from the shipping pouch and place "EMPTY" label on one of the metal plates on the outer container
4. Seal the shipping pouch containing the return label, remove sticker backing, and place return label on the other metal plate on the outer container
5. Close the outer container lid and lock the latch by turning the key to the right
6. Place LN<sub>2</sub> dry vapor shipper in scheduled pickup location or contact Cell Therapy 360<sup>®</sup> at 1-888-805-4555 to schedule a pickup

NOTE: Cassettes should be disposed of on site after administration of ABECMA<sup>®</sup>.

### IMPORTANT SAFETY INFORMATION (cont'd)

**Secondary Malignancies (cont'd):** T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes.

Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy.

**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.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Transition Back to Primary Oncologist

### Considerations<sup>1,9</sup>

After at least 2 weeks of monitoring, the patient may return to the primary oncologist for continued monitoring and routine care appointments. Consider the following before returning your patients to home care:

- **Before transitioning care**, regularly meet with your patients to discuss the treatment they received, side effects, medications, infection prevention, and immunization recommendations
- **Provide** updated medical records and confirm home care is appropriate
- **Transition care** back to the primary oncologist or hematologist within 7 days



### IMPORTANT SAFETY INFORMATION (cont'd)

#### Warnings and Precautions:

**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%). 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.

**Cytokine Release Syndrome (CRS):** CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including  $\geq$  Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) 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 63 days). In the pooled studies, the rate of  $\geq$ Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10<sup>6</sup> CAR-positive T cells.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

## Long-Term Monitoring

### Warnings and precautions include<sup>1</sup>:

- **CRS:** CRS, including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA<sup>®</sup>. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids
- **Neurologic toxicity:** Neurologic toxicity, 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
- **HLH/MAS:** HLH/MAS, including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or neurologic toxicity
- **Prolonged cytopenias:** Prolonged cytopenia with bleeding and infection, including fatal outcomes, occurred following treatment with ABECMA. Patients may exhibit Grade 3 or higher cytopenias for several weeks following pretreatment and ABECMA infusion. Monitor complete blood counts prior to and after ABECMA infusion

### IMPORTANT SAFETY INFORMATION (cont'd)

#### Warnings and Precautions (cont'd):

**Cytokine Release Syndrome (CRS) (cont'd):** The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, multiple organ dysfunction syndrome and HLH/MAS.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

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 10<sup>6</sup> CAR-positive T cells, 76% (54/71) of patients received 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 10<sup>6</sup> 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.

Monitor patients at least daily for 7 days following ABECMA infusion for signs or symptoms of CRS. Continue to monitor patients for signs and symptoms of CRS for at least 2 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).

- **Hypersensitivity reactions:** Monitor for hypersensitivity reactions during infusion
- **Infections:** Monitor patients for signs and symptoms of infection; treat appropriately
- **Hypogammaglobulinemia:** Monitor immunoglobulin levels after treatment. Manage using infection precautions, antibiotic or antiviral prophylaxis, and immunoglobulin replacement
- **Use of live vaccines:** Not recommended for at least 6 weeks prior to lymphodepleting chemotherapy, during treatment with ABECMA, and until immune recovery following treatment
- **Secondary malignancies:** Monitor life-long. In the event that a secondary malignancy occurs, contact Bristol Myers Squibb at 1-888-805-4555 to obtain instructions on patient samples to collect for testing of secondary malignancy of T cell origin
- **Effects on ability to drive and use machines:** Advise patients to refrain from driving or operating heavy or potentially dangerous machines for at least 2 weeks after ABECMA administration

## IMPORTANT SAFETY INFORMATION (cont'd)

**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% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10<sup>6</sup> CAR-positive T cells and 300 to 460 x 10<sup>6</sup> CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) 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.

Please see additional Important Safety Information throughout and click here for full [Prescribing Information](#), including **Boxed WARNINGS** and [Medication Guide](#).



Pre-infusion

## INDICATION

ABECMA (idecabtagene vicleucel) 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.

## IMPORTANT SAFETY INFORMATION

### WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA and SECONDARY HEMATOLOGICAL 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.
- 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.
- 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.
- Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA.

Infusion

Please see additional Important Safety Information throughout and click here for full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

**References:** 1. ABECMA [package insert]. Summit, NJ: Bristol-Myers Squibb Company; 2024. 2. Cho S-F, Anderson KC, Tai Y-T. Targeting B cell maturation antigen (BCMA) in multiple myeloma: potential uses of BCMA-based immunotherapy. *Front Immunol.* 2018;9(1821). doi:10.3389/fimmu.2018.01821 3. Rodriguez-Otero P, Ailawadhi S, Arnulf B, et al. Ide-cel or standard regimens in relapsed and refractory multiple myeloma. *N Engl J Med.* 2023;388(11):1002-1014. doi:10.1056/NEJMoa2213614 4. Data on file. US cell therapy operational talking points & FAQs. Princeton, NJ: Bristol-Myers Squibb Company; Feb 2024. 5. Rodriguez-Otero P, Ailawadhi S, Arnulf B, et al. Ide-cel or standard regimens in relapsed and refractory multiple myeloma. *N Engl J Med.* 2023;388(11)(protocol):1002-1014. doi:10.1056/NEJMoa2213614 6. Data on file. BMS-REF-IDC-0055. Princeton, NJ: Bristol-Myers Squibb Company; August 2024. 7. Data on file. IDEC 004. Princeton, NJ: Bristol-Myers Squibb Company; 2021. 8. Data on file. BMS-REF-IDC-0045. Princeton, NJ: Bristol-Myers Squibb Company; September 2024. 9. Farowich W. Patient discharge process following immune effector cell therapy. Abstract presented at: Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR; February 22, 2020; Orlando, Florida.

Post infusion