NEW DRUG APPROVAL

Brand Name	Abecma®
Generic Name	idecabtagene vicleucel
Drug Manufacturer	Celgene Corporation, a Bristol-Myers Squibb Company

New Drug Approval

FDA Approval Date: March 26, 2021

Review Designation: Orphan, Breakthrough Therapy, Priority

Type of Review: Biologics License Application (BLA): 125736

Dispensing Restrictions: Limited Distribution

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Multiple myeloma (MM) occurs when plasma cells in the bone marrow proliferate. This causes accumulation of the clonal plasma cells in the bone marrow, which crowd out other blood cell lines and can result in skeletal destruction, osteolytic lesions, osteopenia, fractures, hypercalcemia, renal insufficiency, anemia, infections, and death.

The estimated incidence rate in the United States is 7 per 100,000 persons, with approximately 32,270 new cases in 2020. The median overall survival (OS) is less than 7 years for patients with a revised International Staging System (r-ISS) stage II disease, and 3.6 years for patients with stage III disease. The median age at diagnosis is 69 years. With the aging population, the number of cases of MM is expected to continue to increase.

In the United States in 2021, there will be an estimated 34,920 adults (19,320 men and 15,600 women) diagnosed with multiple myeloma. It is estimated that there will be about 12,410 deaths from multiple myeloma during 2021.

Efficacy

In the Phase 2, open-label, single-arm, multicenter KarMMa study, 135 patients underwent leukapheresis for the target dose range of 300 × 106 to 450 × 106 CAR-positive T-cells.

- 11 (8%) patients did not receive the CAR-positive T cells either due to death (n = 2), adverse event (n = 1), disease progression (n = 1), consent withdrawal (n = 3), physician decision (n = 3), or inability to manufacture product (manufacturing failure [n = 1]). Two patients died after receiving lymphodepletion and prior to receiving Abecma®. Deaths were from septic shock and general physical health deterioration.
- 24 (18%) patients either received Abecma® outside of the dose range of 300 to 460 × 106 CAR-positive T cells (n = 23) or received CAR-positive T cells that did not meet product release specifications for Abecma® (nonconforming product; n = 1).
- The evaluable population for efficacy analyses consisted of the 100 patients (74%) who received Abecma® in the dose range of 300 to 460 × 106 CAR-positive T cells. Table 1 presents the efficacy results in these patients, and Table 2 provides a summary of the KarMMa study.

Table 1. Efficacy Results for 100 Evaluable Patients	
	Abecma-Treated Population (300 to 460 × 10^6 CAR-Positive T Cells) (N = 100)
Overall Response Rate (sCR + VGPR + PR), n (%) 95% CI	72 (72) 62, 81
sCR, n (%) 95% CI	28 (28) 19, 38
VGPR, n (%) 95% CI	25 (25) 17, 35
PR, n (%) 95% CI	19 (19) 12, 28
Minimal Residual Disease (MRD) Negativity Rate	
MRD negativity rate in all treated patients (n = 100), n (%) 95% CI	21 (21) 13, 30
MRD negativity rate in patients achieving CR or sCR status (n = 28), n (%) 95% CI	21 (75) 55, 89
Duration of Response	
Duration of response (PR or better), n Median (months) 95% CI	72 11.0 10.3, 11.4
Duration of response for sCR, n Median (months) 95% CI	28 19.0 11.4, not estimable
Median follow-up for duration of response (DOR)	10.7 months

Source: Abecma Prescribing Information

Abbreviations: CAR, chimeric antigen receptor; CI, confidence interval; CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Table 2. KarMMa (NCT03361748): Study Design Summary	
Study Population	• Median patient age of 100 efficacy-evaluable patients: 62 years (range, 33–78 years) • Median time since diagnosis: 6 years (range, 1–18 years) • 60% male • Median number of prior therapies: 6 (range, 3–16) • 95% of patients previously underwent at least 1 autologous hematopoietic stem cell transplant • 87% of patients required bridging therapy • 89% of patients had double-refractory disease, 85% were triple refractory, 88% had received 4 of more prior lines of therapy, and 26% were penta-refractory • 94% were refractory to anti-CD38 antibodies
Inclusion Criteria	• ≥18 years of age • Must have received at least 3 prior MM treatment regimens. Note: Induction with or without hematopoietic stem cell transplant and with or without maintenance therapy is considered a single regimen • Must have undergone at least 2 consecutive cycles of treatment for each regimen, unless a partial response (PR) was the best response to the regimen • Must have received a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody • Must be refractory to the last treatment regimen • Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
Interventions	• bb2121 autologous CAR T cells were infused at a dose ranging from 15 to 45 × 10^7 CAR+ T cells after patients received lymphodepleting chemotherapy. • A total of 140 patients were enrolled in the study, with 128 patients receiving an infusion. • 100 patients who received product in the dose range of 300–460 x 10^6 CAR+ T cells were evaluable for efficacy analyses. • Median time from leukapheresis to product availability was 33 days (range, 26–49 days).

Endpoints	• **Primary outcome:** overall response rate (ORR) (percentage of subjects who achieved PR)
	• **Secondary outcomes:**
	  ○ Complete response (CR) rate
	  ○ Time to response
	  ○ Duration of response (DOR)
	  ○ Progression-free survival (PFS)
	  ○ Time to progression
	  ○ Overall survival (OS)
	  ○ Adverse events

Efficacy Results	• Median time to response was 30 days. • Remission in the sCR population lasted for 12 months or more in 65% of patients. • Median PFS was 8.8 months overall; among patients with a CR or better, the PFS was 20.2 months. • Median OS was 19.4 months, and at 12 months, the OS rate was 78% (OS data are still immature).

Safety

ADVERSE EVENTS

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

The most common laboratory adverse reactions (incidence greater than or equal to 50%) include neutropenia, leukopenia, lymphopenia, thrombocytopenia, and anemia.

WARNINGS & PRECAUTIONS

- Hypersensitivity Reactions: Monitor for hypersensitivity reactions during infusion.
- Infections: Monitor patients for signs and symptoms of infection; treat appropriately.
- Prolonged Cytopenias: Patients may exhibit prolonged Grade 3 or higher cytopenias following Abecma® infusion. Monitor blood counts prior to and after Abecma® infusion.
- Hypogammaglobulinemia: Monitor and consider immunoglobulin replacement therapy.
- Secondary Malignancies.
- Effects on Ability to Drive and Use Machines: Advise patients to refrain from driving or operating heavy or potentially dangerous machines for at least 8 weeks after Abecma® administration.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS OF ACTION

Abecma® is a chimeric antigen receptor (CAR)-positive T cell therapy targeting B-cell maturation antigen (BCMA), which is expressed on the surface of normal and malignant plasma cells. The CAR construct includes an anti-BCMA scFv-targeting domain for antigen specificity, a transmembrane domain, a CD3-zeta T cell activation domain, and a 4-1BB costimulatory domain. Antigen-specific activation of Abecma® results in CAR-positive T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells.

Dose & Administration

ADULTS

300 to 460 x 10^6 CAR-positive T-cells as a single IV dose.

PEDIATRICS

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

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

- Abecma® is a cell suspension for intravenous infusion.
- A single dose of Abecma® contains a cell suspension of 300 to 460 x 10^6 CAR-positive T cells in one or more infusion bags.