

Category

Best Biotechnology Product

Drug / Device Name

CARVYKTI® (ciltacabtagene autoleucel)

Compound/ Tech Name

ciltacabtagene autoleucel

Trade Name

CARVYKTI®

Date of Approval

2022-02-28

Indications

CARVYKTI® is a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR)-T cell therapy approved in the United States of America for the treatment of adult patients with relapsed or refractory MM after 4 or more prior lines of therapy including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and an anti CD38 monoclonal antibody.

In the European Union, CARVYKTI® has conditional marketing authorization for the treatment of adult patients with relapsed or refractory MM after 3 or more prior therapies including a PI, an IMiD, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.

CARVYKTI® is indicated in Korea for the treatment of adult patients with relapsed or refractory MM who previously received at least 4 prior therapies including a PI, an IMiD, and an anti-CD38 antibody.

In Japan, CARVYKTI® is approved for the treatment of patients with MM who have received 3 or more lines of therapy including an IMiD, a PI, and an anti-CD38 monoclonal antibody, and in whom MM has not responded to or has relapsed following the most recent therapy.

Therapeutic Categories

Oncology: multiple myeloma (MM)

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- Submission_CARVYKTI_Prix Galien_Section 1.pdf

Background information and need for drug/device

Multiple myeloma (MM) is a hematologic malignancy, long considered to be incurable, that accounts for 1.8% of all newly diagnosed cancers in the U.S. Despite advancements in MM treatments over the last two decades, the 5-year survival rate remains under 60%; with each relapse, MM becomes nonresponsive to more of the existing therapies. Patients rapidly reach fourth and fifth treatment lines, at which point they have few remaining effective treatment options and suffer poor outcomes, as

reflected by a median progression-free survival under 5 months. CARVYKTI®, a bispecific BCMA-directed CAR-T therapy, has the potential to address this unmet need.

CARVYKTI® was approved in the U.S. in 2022 for treatment of relapsed or refractory MM (RRMM) after 4 or more lines of therapy including a proteasome inhibitor (PI), immunomodulatory agent (IMiD), and anti-CD38 monoclonal antibody. CARVYKTI® also has conditional authorization in the EU to treat RRMM after 3 or more therapies including a PI, IMiD, and anti-CD38 antibody after progression on the last therapy; and in Japan to treat MM after 3 or more lines including an IMiD, PI, and anti-CD38 antibody in patients whose MM did not respond to or relapsed after the most recent therapy.

CARVYKTI® is differentiated by its CAR, which contains two different antigen-binding antibodies designed to confer avidity. CARVYKTI® is further distinguished by high rates of deep treatment responses and long-lasting progression-free survival in patients with heavily pretreated RRMM, with safety generally consistent with other CAR-T therapies, and potentially improved tolerability when used earlier in treatment.

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History of the development of the drug/device

CARVYKTI® is a BCMA-directed chimeric antigen receptor (CAR)-T cell therapy. By contrast with the therapeutic targets of earlier multiple myeloma (MM) treatments, BCMA is selectively expressed by the B cell lineage and overexpressed by MM cells – a characteristic that may help limit on-target off-tumor toxicities. CAR-T therapies are a relatively new drug class that combines the effector function of T cells with the ability of antibodies to bind, with high specificity, predefined targets without the MHC restriction of T cells.

The CARVYKTI clinical development plan comprises studies spanning the MM treatment continuum, reflecting the goal of transforming the patient treatment journey from diagnosis, potentially leading to cure in some patients.

Data from the phase 1 LEGEND-2 study, the first clinical trial of LCAR-B38M CAR-T cells, which express the same CAR construct as ciltacabtagene autoleucel (cilta-cel; CARVYKTI®), showed significant rates, depths, and durability of treatment responses and long-term survival outcomes in patients with heavily pretreated RRMM. Based on results from LEGEND-2, the pivotal phase 1b/2 CARTITUDE-1 trial was initiated. CARTITUDE-1 confirmed the efficacy and the safety profile observed in LEGEND-2 and was the basis for the approval of CARVYKTI® in the U.S. and other regions.

In patients with lenalidomide-refractory RRMM after 1–3 lines of therapy, the phase 3 CARTITUDE-4 trial recently showed that cilta-cel led to more and deeper treatment responses and significantly prolonged progression-free survival compared with standard of care regimens. Cilta-cel will be further evaluated in patients with newly diagnosed MM in the CARTITUDE-5 and CARTITUDE-6 studies.

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Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

CARVYKTI® is structurally differentiated by its chimeric antigen receptor (CAR) with 2 BCMA-directed antigen-binding domains. The CAR also possesses 4-1BB costimulatory and CD3ζ signaling domains for optimized T cell activation and proliferation. 4-1BB may also stimulate CD8+ central memory T cell generation and proliferation – translational data show this cell type's enrichment in the CARVYKTI® drug product – and improve CAR-T cell persistence.

Further distinguishing CARVYKTI® are high rates of deep and long-lasting treatment responses and long progression-free survival (PFS) after a single infusion in patients with heavily pretreated relapsed/refractory MM. The phase 1 LEGEND-2 and phase 1b/2, pivotal CARTITUDE-1 studies suggest the potential of CARVYKTI® to improve outcomes in patients who have limited benefit from standard of care (SOC) treatments; the long-term outcomes highlight the possibility of cure in some patients. CARVYKTI® also improves quality of life, in part through long treatment-free periods patients can have with CARVYKTI® compared with continuously dosed therapies.

Moreover, CARVYKTI® is demonstrating it can benefit patients along the treatment continuum and across treatment settings. CARTITUDE-2 (cohort C) showed that despite prior anti-BCMA exposure, patients can still respond to CARVYKTI®. Recent data from the randomized phase 3 CARTITUDE-4 study show CARVYKTI® has superior efficacy – including significant prolongation of PFS – versus SOC as early as after first relapse and potentially better tolerability in earlier lines. CARTITUDE-5 and CARTITUDE-6, in newly diagnosed MM, are evaluating the ability of CARVYKTI® to transform patients' treatment journeys starting at diagnosis and aim to displace SOC, including stem cell transplant in eligible patients.

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Please provide appropriate references (ie Pubmed links)

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