Category

Best Biotechnology Product

General Information

Company Name *

Johnson & Johnson Services, Inc.

Product/Solution Name *

CARVYKTI® (ciltacabtagene autoleucel)

Compound/Tech Name*

ciltacabtagene autoleucel

Trade Name *

CARVYKTI®

Corporate Name *

Johnson & Johnson

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 for the treatment of adult patients with relapsed or refractory MM who have received at least 1 prior line of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), and are refractory to lenalidomide.

In the European Union, CARVYKTI has marketing authorization for the treatment of adult patients with relapsed and refractory MM, who have received at least 1 prior therapy, including a PI and an IMiD, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide.

In Brazil, CARVYKTI is approved for the treatment of adult patients with MM, who previously received a PI and are refractory to lenalidomide, as well as adult patients with relapsed or refractory MM, who previously received a PI, an IMiD, and anti-CD38 antibody.

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Therapeutic Areas *

Oncology: multiple myeloma (MM)

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- Prix Galien_CARVYKTI_1_CategoryProduct.pdf

Background information and need for drug / device
(please be as specific as possible in your description; limit 500 words)

Multiple myeloma (MM) is a hematologic malignancy, long considered to be incurable, that accounts for 1.8% of all newly diagnosed cancers in the United States. Despite advancements in MM treatments over the last two decades, the 5-year survival rate remains approximately 60%. Most of the effective treatments are used in frontline settings, but most patients experience relapse after their first treatment and after subsequent lines. At each relapse, MM becomes nonresponsive to more of the existing therapies and patients face poor outcomes with subsequent therapies. Real-world analyses have shown that the median treatment duration is less than 5 months for each of the first 5 lines of therapy and that median progression-free survival is under 5 months in heavily pretreated patients. CARVYKTI®, a biepitopic BCMA-directed CAR-T therapy, has the potential to address the unmet need for more therapies that are effective as early as after first relapse.

CARVYKTI® was first approved in 2022 as treatment for heavily pretreated relapsed or refractory MM (RRMM). In 2024, CARVYKTI® became the first and only BCMA-directed CAR-T therapy approved in the United States for treatment of adults patients with RRMM after 1 line of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), and who are refractory to lenalidomide. CARVYKTI® also has marketing authorization in the European Union to treat adult patients who have RRMM after at least 1 prior line, including a PI and an IMiD, and are refractory to lenalidomide. In Brazil, CARVYKTI® is approved to treat adult patients with MM, who previously received a PI, an IMiD, and anti-CD38 antibody.

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 as early as after first relapse, long-lasting progression-free survival in patients with heavily pretreated RRMM, and a significant progression-free survival benefit compared with standard of care in patients at early stages of RRMM (1-3 prior lines). The strong efficacy is accompanied by a safety profile in earlier lines that is consistent with the known safety profile of CARVYKTI, and potentially improved tolerability when used earlier in treatment.

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History of the development of the solution/product *
(please be as specific as possible in your description; 500 words)

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 drug class that combines the effector functions 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. 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, in which median progression-free survival was 34.9 months, confirmed the efficacy and the safety profile observed in LEGEND-2 and was the basis for the approval of CARVYKTI® in the United States and other regions.

In patients with lenalidomide-refractory RRMM after 1-3 lines of therapy, the phase 3 CARTITUDE-4 trial - the basis for recent label expansions in the United States and the European Union - showed that, alongside a safety profile of manageable adverse events with appropriate supportive therapy, CARVYKTI® led to more and deeper treatment responses and significantly prolonged progression-free survival (59% reduction in the risk of disease progression or death) compared with 2 effective standard of care regimens (daratumumab, pomalidomide, and dexamethasone; and pomalidomide, bortezomib, and dexamethasone). At median 16-month follow-up, median progression free survival was not reached in the CARVYKTI® arm and was 12 months in the standard of care arm. Progression-free survival benefit with CARVYKTI® was seen in all prespecified subgroup analyses and in post hoc subgroup analyses of patients with high-risk disease features. In addition to clinical benefit, CARVYKTI® versus standard of care also led to numerically greater improvements in health-related quality of life and MM-related symptoms; and a higher proportion of patients who received CARVYKTI® versus standard of care reported clinically meaningful improvements from baseline to month 12 in multiple measures of health-related quality of life and MM-related symptoms.

In Cohort D of the multi-cohort phase 2 CARTITUDE-2 trial, CARVYKTI® recently showed promising efficacy and safety in patients who had suboptimal response (did not achieve complete response or better) to frontline autologous stem cell transplant. Adverse events were consistent with the known safety profile of CARVYKTI®.

In the phase 3 CARTITUDE-5 study, CARVYKTI® is being further evaluated versus standard of care in patients with newly diagnosed MM for whom autologous stem cell transplant is not intended; and in the phase 3 CARTITUDE-6 study, CARVYKTI® will be compared with autologous stem cell transplant in patients with newly diagnosed MM.

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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; consistent with this hypothesis, data show enrichment of CD8+ central memory T cells in the CARVYKTI® drug product.

Further distinguishing CARVYKTI® are high rates of deep and long-lasting treatment responses and long progression-free survival after a single infusion in patients with heavily pretreated relapsed/refractory multiple myeloma (RRMM). The phase 1 LEGEND-2 and phase 1b/2, pivotal CARTITUDE-1 studies suggest the potential of CARVYKTI® to improve outcomes in heavily pretreated patients who have limited benefit from standard of care treatments. The registrational, randomized phase 3 CARTITUDE-4 study showed CARVYKTI® has superior efficacy - including significantly prolonging PFS - versus standard of care regimens as early as after first relapse and potentially better tolerability in earlier lines. Based on CARTITUDE-4, CARVYKTI® became the first and only BCMA-directed CAR-T therapy approved in the United States for the treatment of adult patients with RRMM after 1 line of therapy including a proteasome inhibitor and an immunomodulatory agent, and who are refractory to lenalidomide.

CARVYKTI® also improves quality of life in patients with heavily pretreated RRMM and in patients at earlier lines. These improvements were seen in measures of overall health-related quality of life, functioning, and MM-related symptoms. In patients with 1-3 prior lines of therapy quality of life improvements were greater in magnitude and in proportion of patients with clinically meaningful change with CARVYKTI® versus SOC. The treatment-free period afforded by CARVYKTI®, which unlike continuously dose therapies is administered in a single infusion, may also have contributed to improvements in quality of life.

CARVYKTI® is also demonstrating it can benefit patients at other stages of the MM treatment continuum. Recent data from CARTITUDE-2 (cohort D) showed promising efficacy and safety with CARVYKTI® with or without lenalidomide maintenance in patients who had a suboptimal response (did not achieve complete response or better) after frontline autologous stem cell transplant, a patient population with a historically poorer clinical outcomes. CARTITUDE-5 and CARTITUDE-6 aim to transform patients' treatment journeys starting at diagnosis by displacing standard of care at the first line of therapy. In patients with newly diagnosed MM, CARTITUDE-5 is evaluating CARVYKTI® versus standard of care in patients for whom autologous stem cell transplant is not intended and CARTITUDE-6 is comparing CARVYKTI® with autologous stem cell transplant.

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Please provide appropriate references (PubMed, Abstract, Website) *

Please see uploaded PDF for full reference list.

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Attached Files:

- Prix Galien_CARVYKTI_6_References.pdf