CARVYKTI®
(ciltacabtagene autoleucel) Suspension for IV Infusion

CARVYKTI® (ciltacabtagene autoleucel)

Product Handling Guide

This material is designed to help you follow the steps for receipt, storage, handling, thawing, preparation, and administration of CARVYKTI®.

If some of the processes described in this document are performed by other departments or personnel, please share this document accordingly.

Ensure personnel involved in product handling, storage, and infusion steps have been trained according to the institution's practices.

INDICATIONS AND USAGE

CARVYKTI® (ciltacabtagene autoleucel) 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 four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

IMPORTANT SAFETY INFORMATION

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

Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with CARVYKTI®. Do not administer CARVYKTI® to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), which may be fatal or life-threatening, occurred following treatment with CARVYKTI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with CARVYKTI®. Provide supportive care and/or corticosteroids as needed.

Parkinsonism and Guillain-Barré syndrome and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with CARVYKTI®.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKTI®. HLH/MAS can occur with CRS or neurologic toxicities.

Prolonged and/or recurrent cytopenias with bleeding and infection and requirement for stem cell transplantation for hematopoietic recovery occurred following treatment with CARVYKTI®.

Secondary hematological malignancies, including myelodysplastic syndrome and acute myeloid leukemia, have occurred following treatment with CARVYKTI®.

CARVYKTI® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS Program.

Please read Important Safety Information on pages 10-13 and full Prescribing Information, including Boxed Warning, for CARVYKTI®.

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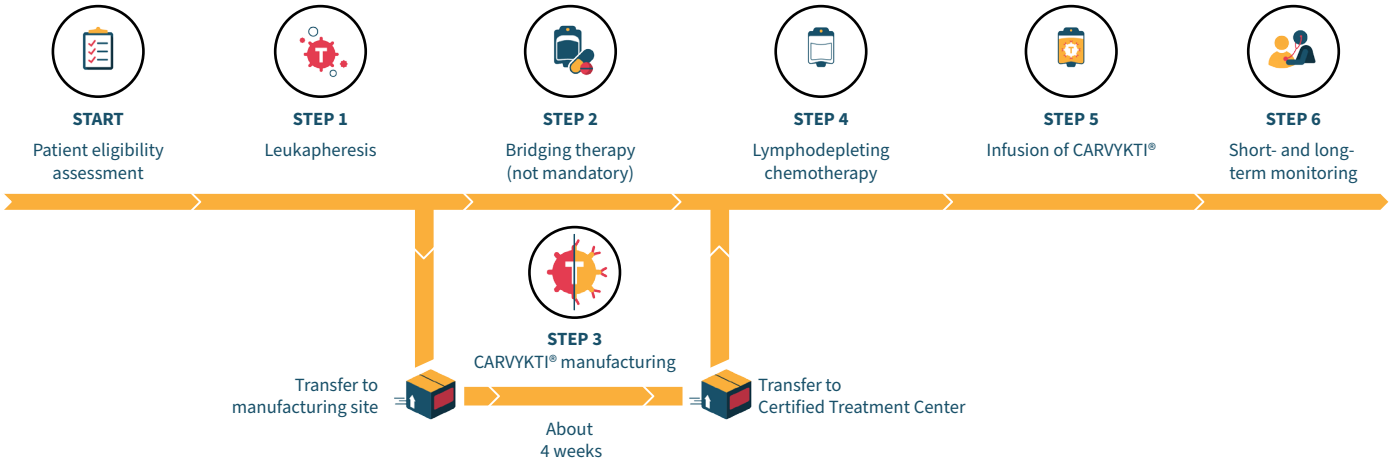
Introduction to CARVYKTI®[1]

- CARVYKTI® is a BCMA-directed, genetically modified autologous T cell immunotherapy, which involves reprogramming a patient's own T cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. The CARVYKTI® CAR protein features two BCMA-targeting single domain antibodies designed to confer high avidity against human BCMA, a 4-1BB co-stimulatory domain and a CD3_zeta (CD3ζ) signaling cytoplasmic domain. Upon binding to BCMA expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells
- CARVYKTI® is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma, after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

The CARVYKTI® Cell Therapy Process

THERE ARE MULTIPLE STEPS INVOLVED IN CAR-T THERAPY



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BCMA=B cell maturation antigen; CAR-T=chimeric antigen receptor-T cell.

Reference: 1. CARVYKTI® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

The CARVYKTI® Process[1]

LEUKAPHERESIS

Leukapheresis involves removing the patient's T cells, after which they will be packaged, cryopreserved, and sent to the CAR-T cell manufacturing facility. Leukapheresis can take 3 to 6 hours and may need to be repeated.

BRIDGING THERAPY

In the pivotal CARTITUDE-1 trial, most patients (75%) treated with ciltacabtagene autoleucel received bridging therapy for control of their multiple myeloma during the manufacturing process. Bridging therapy may take place at a Certified Treatment Center or the patient's local oncology practice.

Preparing the Patient for CARVYKTI® Infusion[1]

LYMPHODEPLETING CHEMOTHERAPY

- Confirm the availability of CARVYKTI® prior to starting the lymphodepleting regimen
- Administer the lymphodepleting regimen of cyclophosphamide 300 mg/m^2 intravenously daily and fludarabine 30 mg/m^2 intravenously daily for 3 days. For dose adjustments in renal impairment, see corresponding manufacturer's prescribing information
- Lymphodepleting regimen must be delayed if a patient has serious adverse reactions from preceding bridging therapies (including clinically significant active infection, cardiac toxicity, and pulmonary toxicity) or active graft versus host disease in patients with prior allogenic stem cell transplant
- Consider repeating lymphodepleting regimen if CARVYKTI® dosing is delayed by more than 14 days and patient has recovered from toxicity of the first lymphodepleting regimen
- Administer CARVYKTI® infusion 2 to 4 days after the completion of the lymphodepleting chemotherapy regimen

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Before Administration[1]

CLINICAL ASSESSMENT PRIOR TO CARVYKTI® INFUSION

CARVYKTI® infusion should be delayed if a patient has any of the following conditions:

- Clinically significant active infection or inflammatory disorders
- Grade ≥3 non-hematologic toxicities of cyclophosphamide and fludarabine conditioning except for Grade 3 nausea, vomiting, diarrhea, or constipation. CARVYKTI® infusion should be delayed until resolution of these events to Grade ≤1

PREMEDICATION

- Administer the following pre-infusion medications to all patients 30 to 60 minutes prior to CARVYKTI® infusion:
  - Antipyretics (oral or intravenous acetaminophen 650 to 1,000 mg)
  - Antihistamine (oral or intravenous diphenhydramine 25 to 50 mg or equivalent)
- Avoid use of prophylactic systemic corticosteroids as their use may interfere with the activity of CARVYKTI®

Dosage and Administration[1]

CARVYKTI® DOSE

- CARVYKTI® is for autologous and intravenous use only
- CARVYKTI® is provided as a single infusion that takes approximately 30 to 60 minutes containing a suspension of chimeric antigen receptor (CAR)+ viable T cells in one infusion bag. The dose is 0.5-1.0×10^6 CAR+ viable T cells per kg of body weight, with a maximum dose of 1×10^8 CAR+ viable T cells per single infusion

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Receipt of CARVYKTI®[1]

- All sites approved for infusion will support required storage conditions for vapor phase of liquid nitrogen
- CARVYKTI® is shipped directly to the cell laboratory or clinical pharmacy associated with the infusion center in the vapor phase of a liquid nitrogen shipper
- Confirm the patient's identity with the patient identifiers on the shipper
- If the patient is not expected to be ready for same-day administration, before the shipper expires, transfer CARVYKTI® to onsite vapor phase of liquid nitrogen storage

Please consult the Cilta-cel CAR-T Receipt & Storage Manual for the specific guidance for receipt and storage requirements for CARVYKTI® as well as training provided to your site.[3]

Storage of CARVYKTI®

- The product must be stored and transported according to the conditions on the label, below -120°C, in a container for cryogenic storage in the vapor phase of LN2[1]
- Handling of the product outside of the cryogenic storage (-120°C) will cause a very rapid rise in temperature and should be minimized/avoided[2]
- Store in the original packaging containing the cassette protecting the infusion bag[1]
- Temperature conditions during on-site storage of CARVYKTI® must be monitored, verified, and recorded on a temperature log or temperature alarm log daily, during site working days[3]
- If a temperature out-of-range event happens at any time during storage, immediately quarantine the product according to the manufacturing requirements (eg, LN2), and contact the local Janssen representative at 1-800-526-7736[3]

Handling and Disposal of CARVYKTI®[1]

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

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LN2=liquid nitrogen.

References: 1. CARVYKTI® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Data on file. **3.** Data on file. Cilta-cel CAR-T Receipt and Storage Manual.

Preparation of CARVYKTI® for Infusion[1]

- Do not thaw the product until it is ready to be used. Coordinate the timing of CARVYKTI® thaw and infusion. Confirm the infusion time in advance and adjust the start time for thaw so that CARVYKTI® is available for infusion when the patient is ready. Once thawed, the CARVYKTI® infusion must be completed within 2.5 hours at room/ambient temperature (20°C to 25°C)
- Prior to thawing the product, confirm that tocilizumab and emergency equipment are available prior to the infusion and during the recovery period

1. Confirm patient identity: Prior to CARVYKTI® preparation, match the patient's identity with the patient identifiers on the CARVYKTI® cassette. Do not remove the CARVYKTI® infusion bag from the cassette if the information on the patient-specific label does not match the intended patient. Contact **Janssen Biotech, Inc.**, at **1-800-526-7736** if there are any discrepancies between the labels and the patient identifiers
2. Once patient identification is confirmed, remove the CARVYKTI® infusion bag from the cassette and check that the patient information on the cassette label matches the patient information on the bag label
3. Inspect the infusion bag for any breaches of container integrity such as breaks or cracks before and after thawing. Do not administer if the bag is compromised; contact **Janssen Biotech, Inc.**, at **1-800-526-7736**
4. Place the infusion bag inside a sealable plastic bag (preferably sterile) prior to thawing
5. Thaw CARVYKTI® at 37°C ±2°C using either a water bath or dry thaw method until there is no visible ice in the infusion bag. Total time from start of thaw until completion of thawing should be no more than 15 minutes
6. Remove the infusion bag from the sealable plastic bag and wipe dry. Gently mix the contents of the bag to disperse clumps of cellular material. If visible cell clumps remain, continue to gently mix the contents of the bag. Small clumps of cellular material should disperse with gentle manual mixing. Do not pre-filter into a different container, wash, spin down, and/or resuspend CARVYKTI® in new media prior to infusion
7. Do not re-freeze or refrigerate thawed product

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Administration of CARVYKTI® [1-4]

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

1. Confirm the patient's identity with the patient identifiers on the infusion bag. Do not infuse CARVYKTI® if the information on the patient-specific label does not match the intended patient
2. Prime the tubing of the infusion set with normal saline prior to infusion
3. Once thawed, administer the entire contents of the CARVYKTI® bag by intravenous infusion within 2.5 hours using infusion sets fitted with an in-line filter
4. Gently mix the contents of the bag during CARVYKTI® infusion to disperse cell clumps
5. After the entire content of the product bag is infused, flush the administration line, inclusive of the in-line filter, with normal saline with a volume equal or greater to the total hold up volume of the primary administration set used, inclusive of the drip tube, to ensure that all product is delivered

- A non-leukocyte depleting filter is commonly referred to as a blood filter. All blood and cell products must be administered through a filter in order to remove cell clots and thrombi. Standard blood filters, with a pore size of 170–260 µm, trap large aggregates and clots
- CARVYKTI® is an engineered T cell product derived from a patient's blood and therefore has been developed to follow standard practices of administration as a blood and cell product. To ensure the engineered T cells are not filtered out during infusion, while preventing potential agglomerates and clots of material from being infused to the patient, a non-leukocyte depleting filter (blood filter) must be used. If agglomerates/thrombi enter the bloodstream, there is a potential for the formation of clots, which can lead to pulmonary embolism
- Blood filters are also available as microagglomerate filters which have a pore size range of 10–40 µm. CARVYKTI® has not been evaluated for administration with microagglomerate filters and therefore they must NOT be used during infusion

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Monitoring After Infusion[1]

- Administer CARVYKTI® at a REMS-Certified Treatment Center
- Monitor patients at least daily for 10 days following CARVYKTI® infusion at a Certified Treatment Center for signs and symptoms of cytokine release syndrome (CRS) and neurologic toxicities. Monitor periodically for 4 weeks for signs and symptoms of delayed neurologic toxicity
- Instruct patients to remain within proximity of the Certified Treatment Center for at least 4 weeks following infusion
- Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following infusion

Accidental Exposure

Accidental exposure to CARVYKTI® must be avoided. Local guidelines on handling of human-derived material should be followed in case of accidental exposure, which may include washing of the contaminated skin and removal of contaminated clothes. Work surfaces and materials which have potentially been in contact with CARVYKTI® must be decontaminated with appropriate disinfectant.

COVID-19[1]

Patients treated with ciltacabtagene autoleucel have an increased risk of fatal COVID-19 infections. Follow institutional guidelines for the vaccination and management of immunocompromised patients with COVID-19.

Reporting of Adverse Reactions

Any adverse reactions and/or quality complaints should be reported.

- In order to improve the traceability of CARVYKTI® the batch/lot number of the administered product should be clearly recorded when reporting an adverse reaction
- When reporting a suspected adverse reaction, please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment date

Report suspected adverse reactions[1]

Janssen Biotech, Inc.: 1-800-JANSSEN (1-800-526-7736)
FDA: 1-800-FDA-1088 (1-800-332-1988)
fda.gov/medwatch

CARVYKTI® is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called CARVYKTI® REMS[1]

CALL 1-844-672-0067 (M-F, 8 AM-8 PM ET)
VISIT CARVYKTIREMS.COM

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Parkinsonism and Guillain-Barré syndrome and their associated complications resulting in fatal or life-threatening reactions have occurred following treatment with CARVYKTI®.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including fatal and life-threatening reactions, occurred in patients following treatment with CARVYKTI®. HLH/MAS can occur with CRS or neurologic toxicities.

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WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS) including fatal or life-threatening reactions, occurred following treatment with CARVYKTI® in 95% (92/97) of patients receiving ciltacabtagene autoleucel. Grade 3 or higher CRS (2019 ASTCT grade) occurred in 5% (5/97) of patients, with Grade 5 CRS reported in 1 patient. The median time to onset of CRS was 7 days (range: 1-12 days). The most common manifestations of CRS included pyrexia (100%), hypotension (43%), increased aspartate aminotransferase (AST) (22%), chills (15%), increased alanine aminotransferase (ALT) (14%) and sinus tachycardia (11%). Grade 3 or higher events associated with CRS included increased AST and ALT, hyperbilirubinemia, hypotension, pyrexia, hypoxia, respiratory failure, acute kidney injury, disseminated intravascular coagulation and hemorrhage, HLH/MAS, angina pectoris, supraventricular and ventricular tachycardia, malaise, myalgias, increased C-reactive protein, ferritin, blood alkaline phosphatase and gamma-glutamyl transferase.

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. One patient with CRS and suspected HLH/MAS developed a fatal retroperitoneal hemorrhage in the setting of thrombocytopenia, coagulopathy and anticoagulation in another ongoing study of CARVYKTI®.

Sixty-nine of 97 (71%) patients received tocilizumab and/or a corticosteroid for CRS after infusion of ciltacabtagene autoleucel. Forty-four (45%) patients received only tocilizumab, of whom 33 (34%) received a single dose and 11 (11%) received more than one dose; 24 patients (25%) received tocilizumab and a corticosteroid, and one patient (1%) received only corticosteroids. Ensure that a minimum of two doses of tocilizumab are available prior to infusion of CARVYKTI®.

Monitor patients at least daily for 10 days following CARVYKTI® infusion at a REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, immediately institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic toxicities, which may be severe, life-threatening or fatal, occurred following treatment with CARVYKTI®. Neurologic toxicities included ICANS, neurologic toxicity with signs and symptoms of parkinsonism, Guillain-Barré Syndrome, immune mediated myelitis, peripheral neuropathies, and cranial nerve palsies. Counsel patients on the signs and symptoms of these neurologic toxicities, and on the delayed nature of onset of some of these toxicities. Instruct patients to seek

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

immediate medical attention for further assessment and management if signs or symptoms of any of these neurologic toxicities occur at any time.

Overall, one or more subtypes of neurologic toxicity described below occurred following ciltacabtagene autoleucel in 26% (25/97) of patients, of which 11% (11/97) of patients experienced Grade 3 or higher events. These subtypes of neurologic toxicities were also observed in two ongoing studies.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Patients may experience fatal or life-threatening ICANS following treatment with CARVYKTI®, including before CRS onset, concurrently with CRS, after CRS resolution, or in the absence of CRS. ICANS occurred in 23% (22/97) of patients receiving ciltacabtagene autoleucel including Grade 3 or 4 events in 3% (3/97) and Grade 5 (fatal) events in 2% (2/97). The median time to onset of ICANS was 8 days (range 1-28 days). All 22 patients with ICANS had CRS. The most frequent (≥5%) manifestation of ICANS included encephalopathy (23%), aphasia (8%) and headache (6%).

Monitor patients at least daily for 10 days following CARVYKTI® infusion at the REMS-certified healthcare facility for signs and symptoms of ICANS. Rule out other causes of ICANS symptoms. Monitor patients for signs or symptoms of ICANS for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Parkinsonism: Of the 25 patients in the CARTITUDE-1 study experiencing any neurotoxicity, six male patients had neurologic toxicity with several signs and symptoms of parkinsonism, distinct from immune effector cell-associated neurotoxicity syndrome (ICANS). Neurologic toxicity with parkinsonism has been reported in other ongoing trials of ciltacabtagene autoleucel. Patients had parkinsonian and non-parkinsonian symptoms that included tremor, bradykinesia, involuntary movements, stereotypy, loss of spontaneous movements, masked facies, apathy, flat affect, fatigue, rigidity, psychomotor retardation, micrographia, dysgraphia, apraxia, lethargy, confusion, somnolence, loss of consciousness, delayed reflexes, hyperreflexia, memory loss, difficulty swallowing, bowel incontinence, falls, stooped posture, shuffling gait, muscle weakness and wasting, motor dysfunction, motor and sensory loss, akinetic mutism, and frontal lobe release signs. The median onset of parkinsonism in the 6 patients in CARTITUDE-1 was 64 days (range 14-914 days) from infusion of ciltacabtagene autoleucel.

Monitor patients for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures. There is limited efficacy information with medications used for the treatment of Parkinson's disease, for the improvement or resolution of parkinsonism symptoms following CARVYKTI® treatment.

Guillain-Barré Syndrome: A fatal outcome following Guillain-Barré Syndrome (GBS) has occurred in another ongoing study of ciltacabtagene autoleucel despite treatment with intravenous immunoglobulin (IVIG). Symptoms reported include those consistent with Miller-Fisher variant of GBS, encephalopathy, motor weakness, speech disturbances and polyradiculoneuritis.

Monitor for GBS. Evaluate patients presenting with peripheral neuropathy for GBS. Consider treatment of GBS with supportive care measures and in conjunction with immunoglobulin and plasma exchange, depending on severity of GBS.

Immune Mediated Myelitis: Grade 3 myelitis has occurred 25 days following treatment in another ongoing study. Symptoms reported included hypoesthesia of the lower extremities and the lower abdomen with impaired sphincter control. Symptoms improved with the use of corticosteroids and intravenous immune globulin. Myelitis was ongoing at the time of death from other cause.

Peripheral Neuropathy: Seven patients in CARTITUDE-1 developed peripheral neuropathy. These neuropathies presented as sensory, motor or sensorimotor neuropathies. Median time of onset of symptoms was 66 days (range 4-914 days), median duration of peripheral neuropathies was 138 days (range 2-692 days) including those with ongoing neuropathy. Patients who experienced peripheral neuropathy also experienced cranial nerve palsies or GBS in other ongoing trials of ciltacabtagene autoleucel. Monitor patients for signs and symptoms of peripheral neuropathies.

Cranial Nerve Palsies: Three patients (3.1%) experienced cranial nerve palsies in CARTITUDE-1. All three patients had 7th cranial nerve palsy; one patient had 5th cranial nerve palsy as well. Median time to onset was 26 days (range 21-101 days) following infusion of ciltacabtagene autoleucel. Occurrence of 3rd and 6th cranial nerve palsy, bilateral 7th cranial nerve palsy, worsening of cranial nerve palsy after improvement, and occurrence of peripheral neuropathy in patients with cranial nerve palsy have also been reported in ongoing trials of ciltacabtagene autoleucel. Monitor patients for signs and symptoms of cranial nerve palsies. Consider management with systemic corticosteroids, depending on the severity and progression of signs and symptoms.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): Fatal HLH occurred in one patient (1%), 99 days after ciltacabtagene autoleucel. The HLH event was preceded by prolonged CRS lasting 97 days. The manifestations of HLH/MAS include hypotension, hypoxia with diffuse alveolar damage, coagulopathy, cytopenia, and multi-organ dysfunction, including renal dysfunction.

One patient with Grade 4 HLH/MAS developed fatal intracerebral and gastrointestinal hemorrhage in the setting of coagulopathy and thrombocytopenia 12 days after treatment in another ongoing study. Patients who develop HLH/MAS have an increased risk of severe bleeding. Monitor hematological parameters in patients with HLH/MAS and transfuse per institutional guidelines.

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

CARVYKTI® REMS: Because of the risk of CRS and neurologic toxicities, CARVYKTI® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CARVYKTI® REMS.

Further information is available at https://www.carvyktirems.com/ or 1-844-672-0067.

Prolonged and Recurrent Cytopenias: Patients may exhibit prolonged and recurrent cytopenias following lymphodepleting chemotherapy and CARVYKTI® infusion. One patient underwent autologous stem cell therapy for hematopoietic reconstitution due to prolonged thrombocytopenia.

In CARTITUDE-1, 30% (29/97) of patients experienced prolonged Grade 3 or 4 neutropenia and 41% (40/97) of patients experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Day 30 following ciltacabtagene autoleucel infusion.

Recurrent Grade 3 or 4 neutropenia, thrombocytopenia, lymphopenia and anemia were seen in 63% (61/97), 19% (18/97), 60% (58/97), and 37% (36/97) after recovery from initial Grade 3 or 4 cytopenia following infusion. After Day 60 following ciltacabtagene autoleucel infusion, 31%, 12% and 6% of patients had a recurrence of Grade 3 or higher lymphopenia, neutropenia and thrombocytopenia, respectively, after initial recovery of their Grade 3 or 4 cytopenia. Eighty-seven percent (84/97) of patients had one, two, or three or more recurrences of Grade 3 or 4 cytopenias after initial recovery of Grade 3 or 4 cytopenia. Eight and 12 patients had Grade 3 or 4 neutropenia and thrombocytopenia, respectively, at the time of death.

Monitor blood counts prior to and after CARVYKTI® infusion. Manage cytopenias with growth factors and blood product transfusion support according to local institutional guidelines.

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

Infections (all grades) occurred in 57 (59%) patients. Grade 3 or 4 infections occurred in 21% (20/97) of patients; Grade 3 or 4 infections with an unspecified pathogen occurred in 15%, viral infections in 7%, bacterial infections in 1%, and fungal infections in 1% of patients. Overall, 5 patients had Grade 5 infections: lung abscess (n=1), sepsis (n=3) and pneumonia (n=1).

Grade 5 infections reported in other studies include bronchopulmonary aspergillosis, pneumocystis jirovecii pneumonia, and CMV colitis (with HSV-1 hepatitis). Another patient developed mycotic aneurysm due to cerebral aspergillosis and died of subarachnoid hemorrhage.

Monitor patients for signs and symptoms of infection before and after CARVYKTI® infusion and treat patients appropriately. Administer prophylactic, pre-emptive and/or therapeutic antimicrobials according to the standard institutional guidelines. Febrile neutropenia was observed in 10% of patients after ciltacabtagene autoleucel 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.

In a randomized controlled study of relapsed or refractory multiple myeloma (CARTITUDE-4), patients treated with ciltacabtagene autoleucel had an increased rate of fatal COVID-19 infections compared to the standard therapy arm. Counsel patients on the importance of prevention measures. Follow institutional guidelines for the vaccination and management of immunocompromised patients with COVID-19.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Viral Reactivation: Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients with hypogammaglobulinemia. Perform screening for Cytomegalovirus (CMV), HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV), or any other infectious agents if clinically indicated in accordance with clinical guidelines before collection of cells for manufacturing. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.

Hypogammaglobulinemia was reported as an adverse event in 12% (12/97) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 92% (89/97) of patients. Monitor immunoglobulin levels after treatment with CARVYKTI® and administer IVIG for IgG <400 mg/dL. Manage 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 following CARVYKTI® 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 CARVYKTI® treatment, and until immune recovery following treatment with CARVYKTI®.

Hypersensitivity Reactions have occurred in 5% (5/97) of patients following ciltacabtagene autoleucel infusion. Serious hypersensitivity reactions, including anaphylaxis, may be due to the dimethyl sulfoxide (DMSO) in CARVYKTI®. Patients should be carefully monitored for 2 hours after infusion for signs and symptoms of severe reaction. Treat promptly and manage appropriately according to the severity of the hypersensitivity reaction.

Secondary Malignancies: Patients treated with CARVYKTI® may develop secondary malignancies. Myeloid neoplasms (five cases of myelodysplastic syndrome, three cases of acute myeloid leukemia and two cases of myelodysplastic syndrome followed by acute myeloid leukemia) occurred in 10% (10/97) of patients in CARTITUDE-1 study following treatment with CARVYKTI®. The median time to onset of myeloid neoplasms was 485 days (range: 162 to 1040 days) after treatment with CARVYKTI®. Nine of these 10 patients died following the development of myeloid neoplasms; four of the 10 cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy. Cases of myelodysplastic syndrome and acute myeloid leukemia have also been reported in the post marketing setting. Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Janssen Biotech, Inc., at 1-800-526-7736 for reporting and to obtain instructions on collection of patient samples.

Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status, seizures, neurocognitive decline, or neuropathy, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following CARVYKTI® infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery during this initial period, and in the event of new onset of any neurologic toxicities.

ADVERSE REACTIONS

The most common non-laboratory adverse reactions (incidence greater than 20%) are pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections of unspecified pathogen, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. The most common laboratory adverse reactions (incidence greater than or equal to 50%) include thrombocytopenia, neutropenia, anemia, aminotransferase elevation, and hypoalbuminemia.

Please read full Prescribing Information, including Boxed Warning, for CARVYKTI®.

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