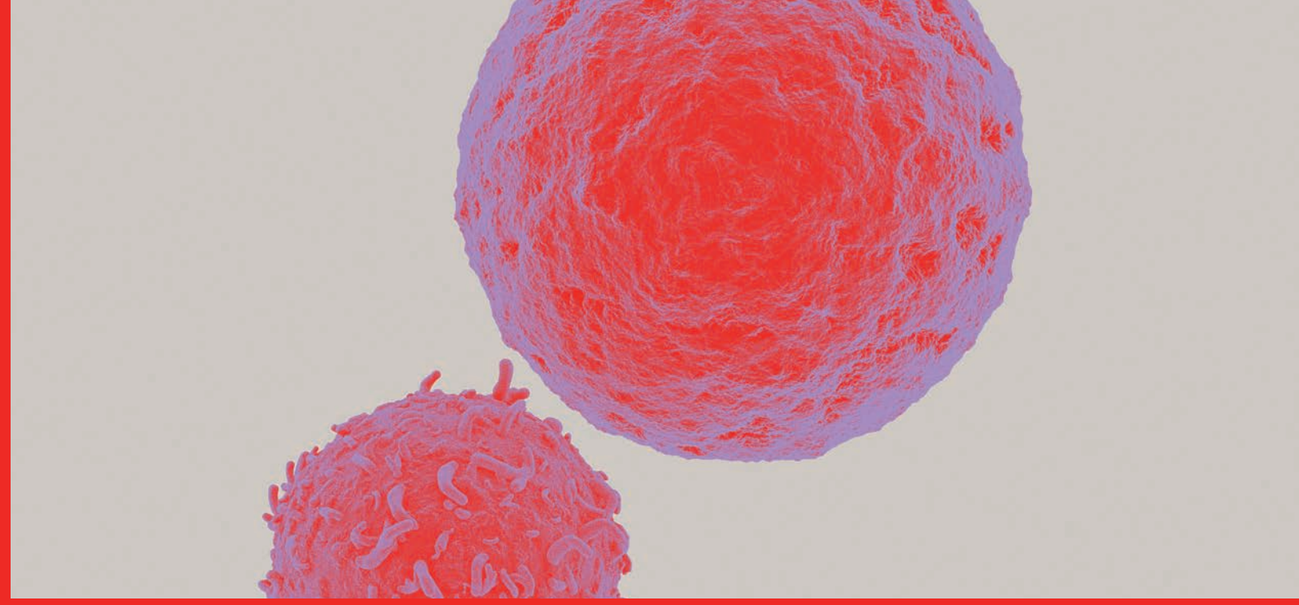


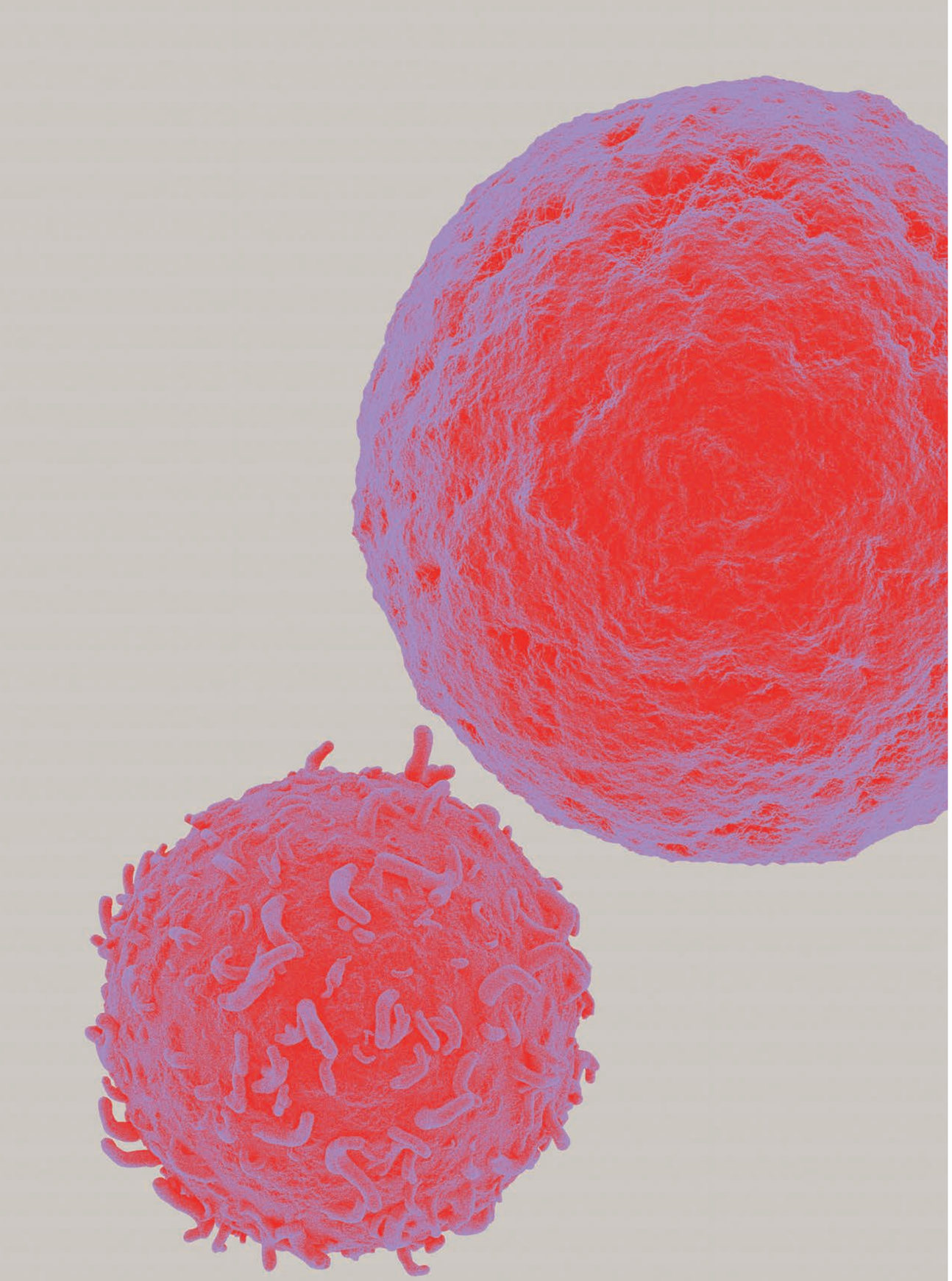
CAR-T Cell Therapy with Ciltacabtagene Autoleucel: Handling Guide

Ciltacabtagene autoleucel
CARVYKTI®

For further information please refer to Summary of product characteristics (SPC)

Johnson&Johnson

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.



Sections with a light grey background are part of the mandatory Risk Management Plan (RMP) for ciltacabtagene autoleucel

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Introduction

This material is aimed at all healthcare professionals (HCPs; e.g. pharmacists, nurses, physicians and ward staff) and any other personnel who are involved in the transport, storage, thawing, preparation or handling of ciltacabtagene autoleucel. Prior to infusion, the qualified treatment centre must have at least 1 dose of tocilizumab available for use in the event of cytokine release syndrome (CRS), with access to an additional dose within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion. Emergency equipment must be available prior to infusion and during the recovery period (see preparation and thawing of ciltacabtagene autoleucel for infusion section).[1] In the case of exceptional use of out-of-specification products, please refer to additional guidance provided by Janssen-Cilag International NV.
If some of the processes described in this document are performed by other departments or personnel, please share this document accordingly.

Introduction to CAR-T cell therapy

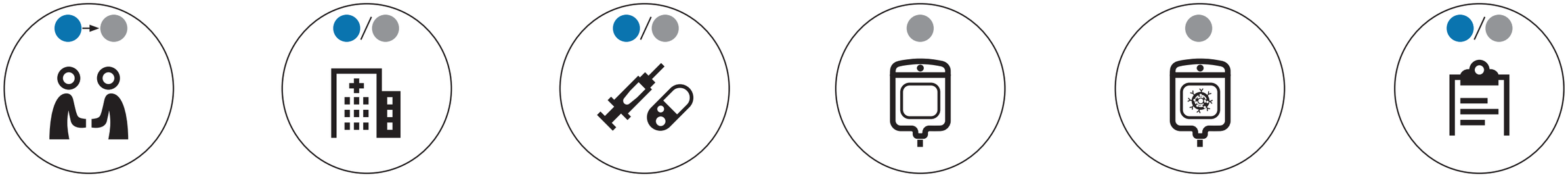
- Ciltacabtagene autoleucel is a B-cell maturation antigen (BCMA)-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. The ciltacabtagene autoleucel 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) signalling cytoplasmic domain. Upon binding to BCMA expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.[1]
- Ciltacabtagene autoleucel is indicated for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least one prior therapy, including an immunomodulatory agent and a proteasome inhibitor, have demonstrated disease progression on the last therapy, and are refractory to lenalidomide.[1]
- After reprogramming, T cells acquire pharmacological activity that gives them the status of drugs.[2]
- Despite its potential, CAR-T cell therapy is associated with adverse events following infusion that can be life-threatening. These include CRS and neurologic toxicities.[1]

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Moreno–Martinez ME, et al. Farm Hosp. 2020;44(1):26–31.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

The CAR-T cell therapy process

There are five steps involved in CAR-T cell therapy:[1]



*In the MMY2001 and MMY3002 studies, the median time from the day after receipt of leukapheresis material at the manufacturing facility to release of medicinal product for infusion was **29 days (range: 23–64 days)** and **44 days (range: 25–127 days)**, respectively. The median time from initial leukapheresis to ciltacabtagene autoleucel infusion was **47 days (range: 41–167 days)** and **79 days (range: 45–246 days)**, respectively.

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Preparing for ciltacabtagene autoleucel infusion

COVID-19

- Please follow all national guidance and adhere to all national restrictions.

Leukapheresis

- Leukapheresis involves removing the patient's white blood cells, after which they will be packaged and sent to the CAR-T cell manufacturing facility. This process can take 3–6 hours and may need to be repeated.[1]
- Please note, patients are required to undergo a wash-out period for certain medications before undergoing leukapheresis. For example, EBMT-JACIE recommendations advise discontinuation of corticosteroids for a minimum of 3 days but ideally 7 days prior to leukapheresis. Please refer to Local SPC.

Bridging therapy

- Patients often receive bridging therapy in the time it takes to manufacture CAR-T cells to control their myeloma.[1] Bridging therapy can take place at the patient's local hospital, and appropriate communication between the CAR-T site and the patient's local medical team is needed in this case.

Pre-treatment (lymphodepleting regimen)

- The availability of ciltacabtagene autoleucel should be confirmed prior to starting the lymphodepleting regimen.[1]
- The 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).[1]
- A lymphodepleting regimen of cyclophosphamide 300 mg/m² intravenous and fludarabine 30 mg/m² intravenous should be administered daily for 3 days. Ciltacabtagene autoleucel infusion should be administered 5 to 7 days after the start of the lymphodepleting regimen.[1] There must be confirmation from the clinician responsible for the patient that the patient is eligible to receive ciltacabtagene autoleucel prior to infusion. This is specific to ciltacabtagene autoleucel; regimens may vary between different CAR-T cell therapies (in terms of dosage and frequency of administration).

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Hayden PJ, et al. Ann Oncol. 2022;33(3):259–275.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

- Common adverse events may include low blood count and infection.[1,2] If resolution of toxicities due to the lymphodepleting regimen to Grade 1 or lower takes more than 14 days, thereby resulting in delays to ciltacabtagene autoleucel dosing, the lymphodepleting regimen should be re-administered after a minimum of 21 days following the first dose of the first lymphodepleting regimen.[3]

Pre-medication[3]

- The following pre-infusion medications should be administered to all patients 30 to 60 minutes prior to ciltacabtagene autoleucel infusion:
  - Antipyretic (oral or intravenous paracetamol 650 to 1,000 mg).
  - Antihistamine (oral or intravenous diphenhydramine 25 to 50 mg or equivalent).
- The use of prophylactic systemic corticosteroids should be avoided as it may interfere with the activity of ciltacabtagene autoleucel.

1. Cyclophosphamide 500 mg Package Leaflet. 2019.
2. Fludarabine 50 mg Package Leaflet. 2023.
3. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Arrival and receipt of ciltacabtagene autoleucel

- Ciltacabtagene autoleucel is supplied as a cell dispersion, in one infusion bag, labelled for the specific patient.[1]
- Confirm materials (shipper label and consignee kit pouch). Photographs may be taken to confirm receipt, or document the condition of the product on arrival.
- Remove and confirm the shipper label with the Chain of Identity (COI) record in the web portal; confirm EVO-IS ID number (last 4 digits) on the airway bill (AWB) matches the EVO-IS ID number on the liquid nitrogen (LN2) shipper lid.
- Check temperature and confirm if there are any deviations in temperature from the prescribed range, or any alarms during transport.
  - In the event of a temperature out-of-range (TOR) event, immediately quarantine the product according to the manufacturing requirements (e.g. LN2) and contact the local Janssen representative on

[Ph. Sadeem Alqahtani; EMEA/ Saudi CAR-T Case manager;

+966 55656 2488; RA-JJ-CART-CaseMngmt@its.jnj.com; SAlqaht2@its.jnj.com] to discuss the potential impact.

  - A TOR report form should be completed and sent electronically to the TOR team.
  - Janssen will complete the bottom of the TOR Report within one working day and indicate whether the product is acceptable for use or not.
  - The completed TOR Report should be filed in your site's appropriate records.

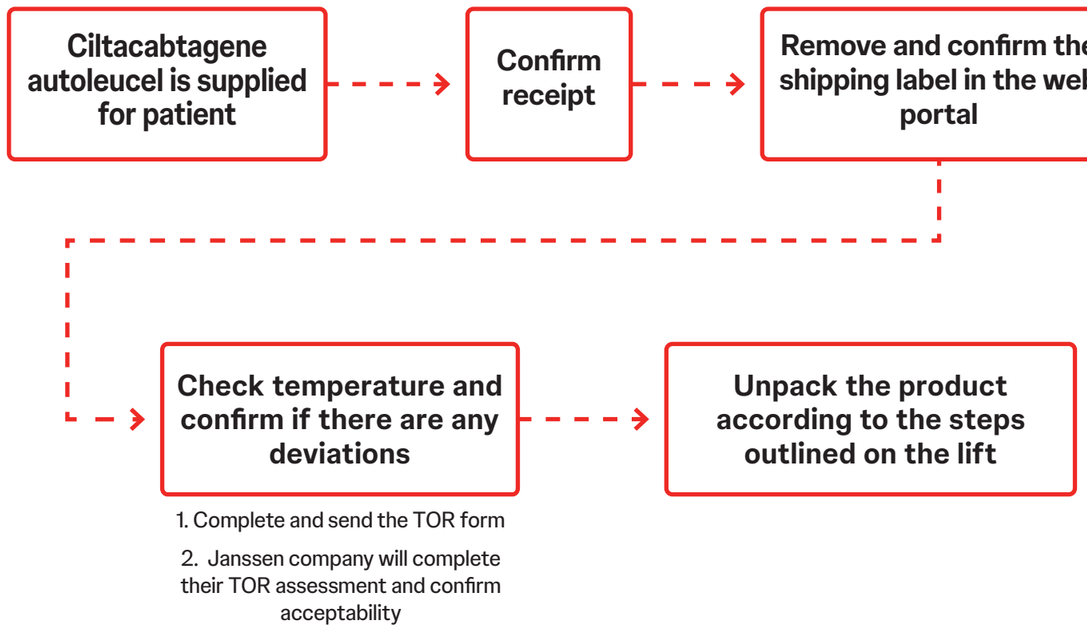
Unpack the product:

- Cut the zip tie and tamper seal to remove shipper lid and lift cassette rack.
- Scan the shipper label to mark unpack start time.
- Cut the tamper evident seal and remove the Tyvek® bag containing the product from the cassette rack.

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025.

- Cut the Tyvek® bag and remove the cassette.
- Confirm the chain of identity (patient name, date of birth [DOB] and single European code-donation identification sequence [SEC-DIS]).
- Place the cassette into LN2 (vapour phase) storage.
- Enter verifications into the web portal and scan the label to mark unpack end time.
- Confirm the thermocouple connector is secured and complete the drug product receipt checklist for site.
- This process should be completed as quickly as possible.

- Enter verifications into the web portal and scan the label to mark unpack end time.
- Confirm the thermocouple connector is secured and complete the drug product receipt checklist for site.
- This process should be completed as quickly as possible.



This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Storage of ciltacabtagene autoleucel

- Ciltacabtagene autoleucel must be stored and transported in the vapour phase of LN2 (≤-120°C) and must remain frozen until the patient is ready for treatment to ensure viable cells are available for patient administration. Thawed medicinal product must not be shaken, refrozen or refrigerated.[1]
- Handling of the product outside of the cryogenic storage (-120°C) will cause a very rapid rise in temperature and should be minimised/avoided.[2]
- The shelf life of ciltacabtagene autoleucel is 9 months.[1]
- Keep infusion bag in the aluminum cryo cassette until ready for thaw and administration.[1]
- Temperature conditions during on-site storage of ciltacabtagene autoleucel must be monitored and recorded.
- The output of the temperature monitoring device must be verified and recorded on a temperature log or temperature alarm log daily, during site working days.
- If a TOR event happens at any time during storage then immediately quarantine the product according to the manufacturing requirements (e.g. LN2), contact the local Janssen representative on [Ph. Sadeem Alqahtani; EMEA/ Saudi CAR-T Case manager;

  +966 55656 2488

  RA-JJ-CART-CaseMngmt@its.jnj.com; SAlqaht2@its.jnj.com]

  and follow the TOR actions detailed on the previous page.

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025. 2. Data on file: RF-167500, 19 April 2021.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Handling ciltacabtagene autoleucel

- This medicinal product contains human blood cells. Healthcare professionals handling ciltacabtagene autoleucel should take appropriate precautions (wearing gloves, protective clothing and eye protection) to avoid potential transmission of infectious diseases.[1]

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

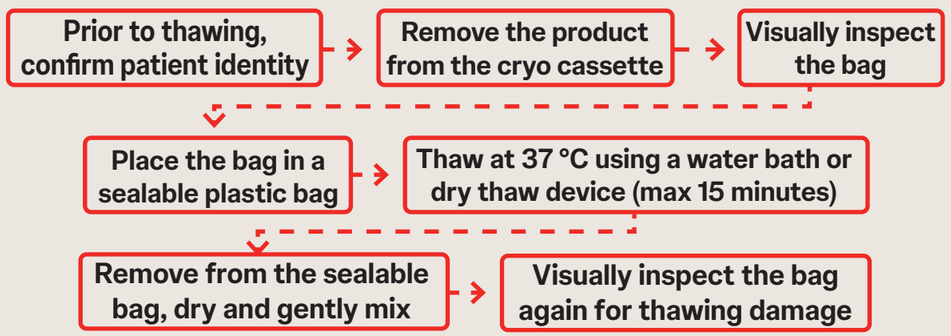
Preparation and thawing of ciltacabtagene autoleucel for infusion

- The medicinal product must not be thawed until it is ready to be used. The timing of ciltacabtagene autoleucel thaw and infusion should be coordinated; the infusion time should be confirmed in advance, and the start time for thaw must be adjusted so that ciltacabtagene autoleucel is available for infusion when the patient is ready. The medicinal product should be administered immediately after thawing and the infusion should be completed within 2.5 hours of thawing.[1]
- Prior to ciltacabtagene autoleucel preparation, patient identity should be confirmed by matching the patient's identity with the patient identifiers on the ciltacabtagene autoleucel cryo cassette and Lot Information Sheet. The ciltacabtagene autoleucel infusion bag should not be removed from the cryo cassette if the information on the patient-specific label does not match the intended patient.[1]
- Once patient identification is confirmed, the ciltacabtagene autoleucel infusion bag should be removed from the cryo cassette.[1]
- The infusion bag should be inspected for any breaches of container integrity such as breaks or cracks before thawing. Do not administer if the bag is compromised and contact Janssen-Cilag International NV.[1] Do not manipulate the bag or contents from its original bag in any way prior to thawing or administration.[2]
- The infusion bag should be placed inside a sealable plastic bag prior to thawing.[1] This is to prevent contamination in the event that the infusion bag breaks during thawing.[2]
- Ciltacabtagene autoleucel should be thawed at 37°C ± 2°C using either a water bath or dry thaw device 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.[1] It is good practice to keep the bag fully submerged during thawing and to keep the open end of the plastic bag out of the water during thawing.[2]
- The thawing process is rapid and continuous monitoring is good practice.[2]

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Data on file: RF-167500, 19 April 2021.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

- The infusion bag should be removed from the sealable plastic bag and wiped dry. The contents of the infusion bag should be gently mixed to disperse clumps of cellular material. If visible cell clumps remain, the contents of the bag should continue to be gently mixed. Small clumps of cellular material should disperse with gentle manual mixing. Ciltacabtagene autoleucel must not be pre-filtered into a different container, washed, spun down, and/or resuspended in new media prior to infusion.[1]
- The bag should be inspected for any signs of damage after thawing. As ciltacabtagene autoleucel is a genetically modified product, any damage to the bag should be reported to Janssen-Cilag International NV and local procedures followed to decontaminate the surrounding area if needed. This is also the case if damage has occurred as a result of mishandling (e.g. if not stored or thawed correctly). Please refer to the supplier's agreement for detailed information on actions to take if the bag is damaged.
- Once thawed: maximum 2.5 hours at room temperature (20°C to 25°C). Ciltacabtagene autoleucel infusion must be administered immediately after thawing and completed within 2.5 hours.[1]
- Once thawed, the medicinal product should not be re-frozen or refrigerated.[1]
- Ciltacabtagene autoleucel should not be irradiated as irradiation could inactivate the medicinal product.[1]
- There is a potential risk of decrease in cell viability due to inappropriate handling or preparation of the medicinal product.[1]
- Prior to infusion, the qualified treatment centre must have at least 1 dose of tocilizumab available for use in the event of CRS, with access to an additional dose within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion. Emergency equipment must be available prior to infusion and during the recovery period.[1]



1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

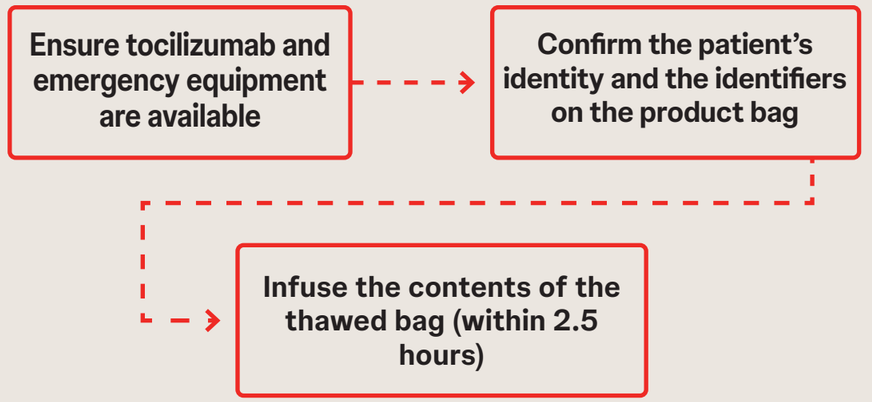
Administration of ciltacabtagene autoleucel

- Ciltacabtagene autoleucel is intended solely for autologous use and must not, under any circumstances, be administered to other patients.[1]
- Ciltacabtagene autoleucel is for intravenous use only.[1]
- Ciltacabtagene autoleucel must be administered in a qualified treatment centre.[1]
- Therapy should be initiated under the direction and supervision of a healthcare professional experienced in the treatment of haematological malignancies and trained for administration and management of patients treated with ciltacabtagene autoleucel.[1]
- Prior to infusion and during the recovery period, ensure tocilizumab and emergency equipment are available for use.[1] In the exceptional case where tocilizumab is not available, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion.[1]
- Confirm the patient's identity with the patient identifiers on the ciltacabtagene autoleucel infusion bag and Lot Information Sheet. Do not infuse ciltacabtagene autoleucel if the information on the patient-specific label does not match the intended patient.[1]
- Once thawed, the entire contents of the ciltacabtagene autoleucel bag should be administered by intravenous infusion within 2.5 hours at room temperature (20°C to 25°C), using infusion sets fitted with an in-line filter. The infusion usually takes less than 60 minutes.[1] Administration can be carried out via central or peripheral catheters. Pump or gravity can be used to infuse.[2]
- Do **NOT** use a leukodepleting filter.[1]
  - 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.[3]

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Data on file: RF-167500, 19 April 2021.
3. Singh S and Kumar A. Biotechnol J. 2009;4:1140–1151.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

  - Ciltacabtagene autoleucel 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 blood stream, there is a potential for the formation of clots, which can lead to pulmonary embolism.
  - Blood filters are also available as microaggregate filters which have a pore size range of 10–40 µm.[1] Ciltacabtagene autoleucel has not been evaluated for administration with microaggregate filters and therefore they must **NOT** be used during infusion.
- Gently mix the contents of the bag during ciltacabtagene autoleucel infusion to disperse cell clumps.[2]
- After the entire content of the product bag is infused, flush the administration line, inclusive of the in-line filter, with sodium chloride 9 mg/mL (0.9%) solution for injection to ensure all medicinal product is delivered.[2]
- Saline must be the only solution used for flushing. Flushing can be done per standard practices using a suitable volume to accomplish this.[3]



1. Mizuno J, J Anesth. 2013;27:645–664.
2. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
3. Data on file: RF-167500, 19 April 2021.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Precautions to be taken for transport and disposal of the medicinal product

- Ciltacabtagene autoleucel should be transported within the facility in closed, break-proof and leak-proof containers.[1]
- Unused medicinal product and all material that has been in contact with ciltacabtagene autoleucel (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling of human-derived material.[1]

Accidental exposure[1]

- In case of accidental exposure local guidelines on handling of human-derived material should be followed. Work surfaces and materials which have potentially been in contact with ciltacabtagene autoleucel must be decontaminated with appropriate disinfectant.

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

Adverse events: CRS

- Potential adverse events associated with CAR-T cell therapy include (among others) CRS and neurologic toxicities.[1]
- Adverse events that occur shortly after treatment (most commonly CRS and neurologic toxicities) will be managed by CAR-T centre HCPs.

Adverse events: CRS

Symptoms[1,*]	• Include, but are not limited to, fever (with or without rigors), chills, hypotension, hypoxia and elevated liver enzymes. Potentially life-threatening complications of CRS may include cardiac dysfunction, neurologic toxicity, and haemophagocytic lymphohistiocytosis (HLH). Patients who develop HLH may have an increased risk of severe bleeding. Evaluation for HLH should be considered in patients with severe or unresponsive CRS.
Incidence[1,*]	• CRS was reported in 83% of patients (n=330); 79% (n=314) of patients had CRS events that were Grade 1 or Grade 2, 4% (n=15) of patients had Grade 3 or Grade 4 CRS events and <1% (n=1) of patients had a Grade 5 CRS event. Ninety-eight percent of patients (n=324) recovered from CRS.
Time to onset[1,*]	• The median time from ciltacabtagene autoleucel infusion (Day 1) to onset of CRS was **7 days (range: 1–23 days)**. Approximately 83% of patients experienced CRS onset after Day 3 of receiving the ciltacabtagene autoleucel infusion.
Duration[1,*]	• Median duration of CRS was **4 days (range: 1–18 days)** for all but one patient, who had a duration of CRS of 97 days, complicated by secondary HLH with a subsequent fatal outcome. Eighty-nine percent of patients had a CRS duration of ≤7 days.
Monitoring	• Patients should be monitored for signs and symptoms of CRS daily for 14 days after the ciltacabtagene autoleucel infusion at a qualified clinical facility, and then periodically for an additional two weeks after ciltacabtagene autoleucel infusion. Patients should be instructed to remain within proximity of a qualified clinical facility for at least 4 weeks following infusion.[1] • Monitoring parameters include: temperature, blood pressure and oxygen saturation.[2] Patients should be counselled to seek immediate medical attention should signs or symptoms of CRS occur at any time.[1]

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).
1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Neelapu SS, et al. Nat Rev Clin Oncol. 2018;15(1)47–62.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Grading	· Please refer to your centre's CAR-T cell standard operating procedure (SOP) or guidelines in order to grade CRS. · The most current grading system for CRS has been developed by the American Society for Transplantation and Cellular Therapies (ASTCT).[1]
Management[2]	· Prior to infusion, the qualified treatment centre must have at least 1 dose of tocilizumab available for use in the event of CRS, with access to an additional dose within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion. · At the first sign of CRS, the patient should be immediately evaluated for hospitalisation and treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids should be instituted as indicated in the ciltacabtagene autoleucel Summary of Product Characteristics (SPC). · Please refer to the ciltacabtagene autoleucel SPC for management of CRS.

Adverse events: Neurologic toxicities

- Neurologic toxicities occur frequently following treatment with ciltacabtagene autoleucel and can be fatal or life-threatening.[2]
- Neurologic toxicities included immune effector cell-associated neurotoxicity syndrome (ICANS), movement and neurocognitive toxicity (MNT) with signs and symptoms of parkinsonism, Guillain-Barré syndrome (GBS), peripheral neuropathies and cranial nerve palsies.[2]
- Neurologic toxicity occurred in 23% of patients (n=90); 6% (n=22) of patients had Grade 3 or Grade 4 neurologic toxicity and 1% (n=3) of patients had Grade 5 neurologic toxicity (one due to ICANS, one due to neurologic toxicity with ongoing parkinsonism and one due to encephalopathy). In addition, eleven patients had fatal outcomes with ongoing neurologic toxicity at the time of death; eight deaths were due to infection (including two deaths in patients with ongoing signs and symptoms of parkinsonism) and one death each due to respiratory failure, cardio-respiratory arrest and intraparenchymal hemorrhage.[2]

1. Lee DW, et al. Biol Blood Marrow Transplant. 2019;25(4):625–638.
2. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

- Baseline neurological characteristics (e.g. behavioural, cognitive, EEG, CT/MRI scans) of patients should be known prior to CAR-T cell infusion to assist with detection of neurologic toxicities following treatment.
- Patients should be counselled on the signs and symptoms of these neurologic toxicities, and on the delayed nature of onset of some of these toxicities.[1]
- Patients should be instructed to seek immediate medical attention for further assessment and management if signs or symptoms of any of these neurologic toxicities occur at any time.[1]

ICANS

Symptoms[1,*]	· Symptoms included: aphasia, slow speech, dysgraphia, encephalopathy, depressed level of consciousness and confusional state.
Incidence[1,*]	· In the pooled studies (N=396), ICANS occurred in 11% of patients (n=45), with 2% (n=8) experiencing Grade 3 or 4 ICANS and <1% (n=1) Grade 5 ICANS.
Time to onset[1,*]	· Patients receiving ciltacabtagene autoleucel may experience fatal or life-threatening ICANS following treatment with ciltacabtagene autoleucel including before CRS onset, concurrent with CRS, following resolution of CRS or in the absence of CRS. · The median time from ciltacabtagene autoleucel infusion to first onset of ICANS was **8 days (range: 2–15 days**, except for 1 patient with onset at 26 days).
Duration[1,*]	· Median duration of ICANS was **3 days (range: 1–29 days**, except for 1 patient who had a subsequent fatal outcome at 40 days).
Monitoring[1]	· Patients should be monitored for signs or symptoms of ICANS for four weeks after infusion. Continue to monitor patients for signs and symptoms of neurologic toxicities after recovery from CRS and/or ICANS. At the first sign of neurologic toxicity including ICANS, neurology evaluation should be considered. Rule out other causes of neurologic symptoms.
Grading	· Please refer to your centre's CAR-T cell SOP or guidelines in order to grade neurologic toxicity. · The most current grading system for ICANS has been developed by the ASTCT.[2]
Management[1]	· At the first sign of ICANS, the patient should be immediately evaluated for hospitalisation and treatment instituted with supportive care. · Please refer to the ciltacabtagene autoleucel SPC for management of neurologic toxicities.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025
2. Lee DW, et al. Biol Blood Marrow Transplant. 2019;25(4):625–638.

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Movement and neurocognitive toxicity (MNT) with signs and symptoms of parkinsonism

Symptoms[1,*]	• A cluster of symptoms with variable onset spanning more than one symptom domain was observed, including movement (e.g. micrographia, tremor, bradykinesia, rigidity, stooped posture, shuffling gait), cognitive (e.g. memory loss, disturbance in attention, confusion), and personality change (e.g. reduced facial expression, flat affect, masked facies, apathy), often with subtle onset (e.g. micrographia, flat affect), that in some patients progressed to an inability to work or care for oneself.
Incidence[1,*]	• Of the 90 patients in the pooled studies (N=396) experiencing any neurotoxicity, nine male patients had neurologic toxicity with several signs and symptoms of parkinsonism, distinct from ICANS. The maximum toxicity grades of parkinsonism were: Grade 1 (n=1), Grade 2 (n=2), Grade 3 (n=6).
Time to onset[1,*]	• The median onset of parkinsonism was **38.0 days (range: 14–914 days)** from infusion of ciltacabtagene autoleucel.
Duration[1,*]	• One patient (Grade 3) died of neurologic toxicity with ongoing parkinsonism 247 days after administration of ciltacabtagene autoleucel. • Two patients (Grade 2 and Grade 3) with ongoing parkinsonism died of infectious causes 162 and 119 days after administration of ciltacabtagene autoleucel. • One patient recovered (Grade 3). • In the remaining 5 patients, symptoms of parkinsonism were ongoing up to 996 days after administration of ciltacabtagene autoleucel.
Risk factors[1,*]	• All 9 patients had a history of prior CRS (n=1 Grade 1; n=6 Grade 2; n=1 Grade 3; n=1 Grade 4), while 6 of 9 patients had prior ICANS (n=5 Grade 1; n=1 Grade 3).
Monitoring and management[1]	• Patients should be monitored for signs and symptoms of parkinsonism that may be delayed in onset and managed with supportive care measures.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).
1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

Guillain-Barré syndrome (GBS)

Symptoms[1,*]	• Symptoms reported include those consistent with Miller-Fisher variant of GBS, motor weakness, speech disturbances, and polyradiculoneuritis.
Incidence[1,*]	• In the pooled studies (N=396), one patient was reported to have GBS after treatment with ciltacabtagene autoleucel.
Duration[1,*]	• Although GBS symptoms improved after receiving treatment with steroids and intravenous immunoglobulin (IVIG), the patient died 139 days after administration of ciltacabtagene autoleucel due to encephalopathy post gastroenteritis with ongoing GBS symptoms.
Monitoring[1]	• Patients should be monitored for GBS. Patients presenting with peripheral neuropathy should be evaluated for GBS.
Management[1]	• Treatment with IVIG and escalation to plasmapheresis should be considered, depending on toxicity severity.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).
1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Peripheral neuropathy

Incidence[1,*]	· In the pooled studies (N=396), 28 patients developed peripheral neuropathy, presenting as sensory, motor, or sensorimotor neuropathies.
Time to onset[1,*]	· Median time of onset of symptoms was **58 days (range: 1–914 days)**.
Duration[1,*]	· Median duration of peripheral neuropathies was **142 days (range: 1–1062 days)** including those with ongoing neuropathy.
Monitoring[1]	· Patients should be monitored for signs and symptoms of peripheral neuropathies.
Management[1]	· Management with short-course systemic corticosteroids should be considered, depending on the severity and progression of signs and symptoms.

Cranial nerve palsies

Incidence[1,*]	· In the pooled studies (N=396), 27 patients experienced cranial nerve palsies. · Occurrence of 7th, 3rd, 5th, and 6th cranial nerve palsy, some of which were bilateral, worsening of cranial nerve palsy after improvement, and occurrence of peripheral neuropathy in patients with cranial nerve palsy have been reported in trials of ciltacabtagene autoleucel.
Time to onset[1,*]	· Median time to onset was **22 days (range: 17–101 days)** following infusion of ciltacabtagene autoleucel.
Duration[1,*]	· Median time to resolution was **61 days (range: 1–443)** following onset of symptoms.
Monitoring[1]	· Patients should be monitored for signs and symptoms of cranial nerve palsies.
Management[1]	· Management with short-course systemic corticosteroids should be considered, depending on the severity and progression of signs and symptoms.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

- Reduction of baseline burden of disease with bridging therapy prior to infusion with ciltacabtagene autoleucel in patients with high tumour burden should be considered, which may mitigate the risk of developing neurologic toxicity. Early detection and aggressive treatment of CRS or ICANS may be important to prevent neurologic toxicity from occurring or worsening.[1]
- Provide intensive care and supportive therapy for severe or life-threatening neurologic toxicities.[1]
- It is advisable that outpatients presenting with neurologic toxicities are transferred to their CAR-T treatment centre. It is important that communication channels are open between the patient's local hospital and the CAR-T treatment centre as delayed admission (when the patient's neurologic toxicities are Grade 3 or higher) could be associated with worse prognostic outcomes.

1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Other adverse events

Adverse events: Prolonged and recurrent cytopenias

Incidence[1,*]

	Grade 3/4 (%) after Day 1 dosing	Initial Grade 3/4 (%) not recovered[a] to ≤Grade 2 by Day 30	Initial Grade 3/4 (%) not recovered[a] to ≤Grade 2 by Day 60	Occurrence of Grade 3/4 (%) >Day 60 (after initial recovery[a] of Grade 3/4)
Thrombocytopenia	191 (48%)	132 (33%)	76 (19%)	14 (4%)
Neutropenia	381 (96%)	111 (28%)	44 (11%)	81 (21%)
Lymphopenia	394 (99%)	97 (25%)	45 (11%)	91 (23%)
Anaemia	184 (47%)	10 (3%)	10 (3%)	26 (7%)

[a]The laboratory result with the worst toxicity grade is used for a calendar day. Recovery definition: must have 2 consecutive Grade ≤2 results on different days if recovery period ≤10 days.
Notes: Lab results assessed after Day 1 until Day 100 for MMY2001 and MMY2003 or Day 112 for MMY3002, or the start of subsequent therapy, whichever occurs first, are included in the analysis.
Thrombocytopenia: Grade 3/4 – Platelets count <50,000 cells/µL.
Neutropenia: Grade 3/4 – Neutrophil count <1,000 cells/µL.
Lymphopenia: Grade 3/4 – Lymphocytes count $<0.5\times10^9$ cells/L.
Anaemia: Grade 3 – Hemoglobin <8g/dL. Grade 4 not defined by laboratory count per NCI-CTCAE v5.
Percentages are based on the number of treated patients.

Time to onset[1]	• Most patients had a median time from infusion to first onset of Grade 3 or 4 cytopenia of less than two weeks with the majority of patients recovering to Grade 2 or lower by Day 30.
Management and monitoring[1]	• Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and ciltacabtagene autoleucel infusion and should be managed according to local guidelines. • Blood counts should be monitored prior to and after ciltacabtagene autoleucel infusion. For thrombocytopenia, supportive care with transfusions should be considered. Prolonged neutropenia has been associated with increased risk of infection. Myeloid growth factors, particularly granulocyte macrophage-colony stimulating factor (GM-CSF), have the potential to worsen CRS symptoms and are not recommended during the first 3 weeks after ciltacabtagene autoleucel or until CRS has resolved.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).
1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

Adverse events: Serious infections and febrile neutropenia

Incidence[1*]	• Infections occurred in 54% of patients (n=213); 18% of patients (n=73) experienced Grade 3 or Grade 4 infections, and fatal infections (COVID-19 pneumonia, pneumonia, sepsis, *Clostridium difficile* colitis, septic shock, bronchopulmonary aspergillosis, pseudomonal sepsis, neutropenic sepsis, and lung abscess) occurred in 4% of patients (n=17). The most frequently reported (≥2%) Grade 3 or higher infections were pneumonia, COVID-19 pneumonia, and sepsis. • Febrile neutropenia was observed in 6% of patients with 2% experiencing serious febrile neutropenia.
Monitoring[1]	• Patients should be monitored for signs and symptoms of infection prior to and during treatment with ciltacabtagene autoleucel and treated appropriately. Infections are known to complicate the course and management of concurrent CRS.
Management[1]	• Prophylactic antimicrobials should be administered according to local guidelines. • Patients with clinically significant active infection should not start ciltacabtagene autoleucel treatment until the infection is controlled. • In the event of febrile neutropenia, infection should be evaluated and managed appropriately with broad-spectrum antibiotics, fluids and other supportive care, as medically indicated. • Patients treated with ciltacabtagene autoleucel may be at an increased risk of severe/fatal COVID-19 infections. Patients should be counselled on the importance of prevention measures.

*Data from pooled studies (N=396): Study MMY2001 (N=106), which included patients from the main Phase 1b/2 cohort (United States; n=97) and an additional cohort (Japan; n=9), Phase 2 Study MMY2003 (N=94) and Phase 3 Study MMY3002 (N=196).
1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

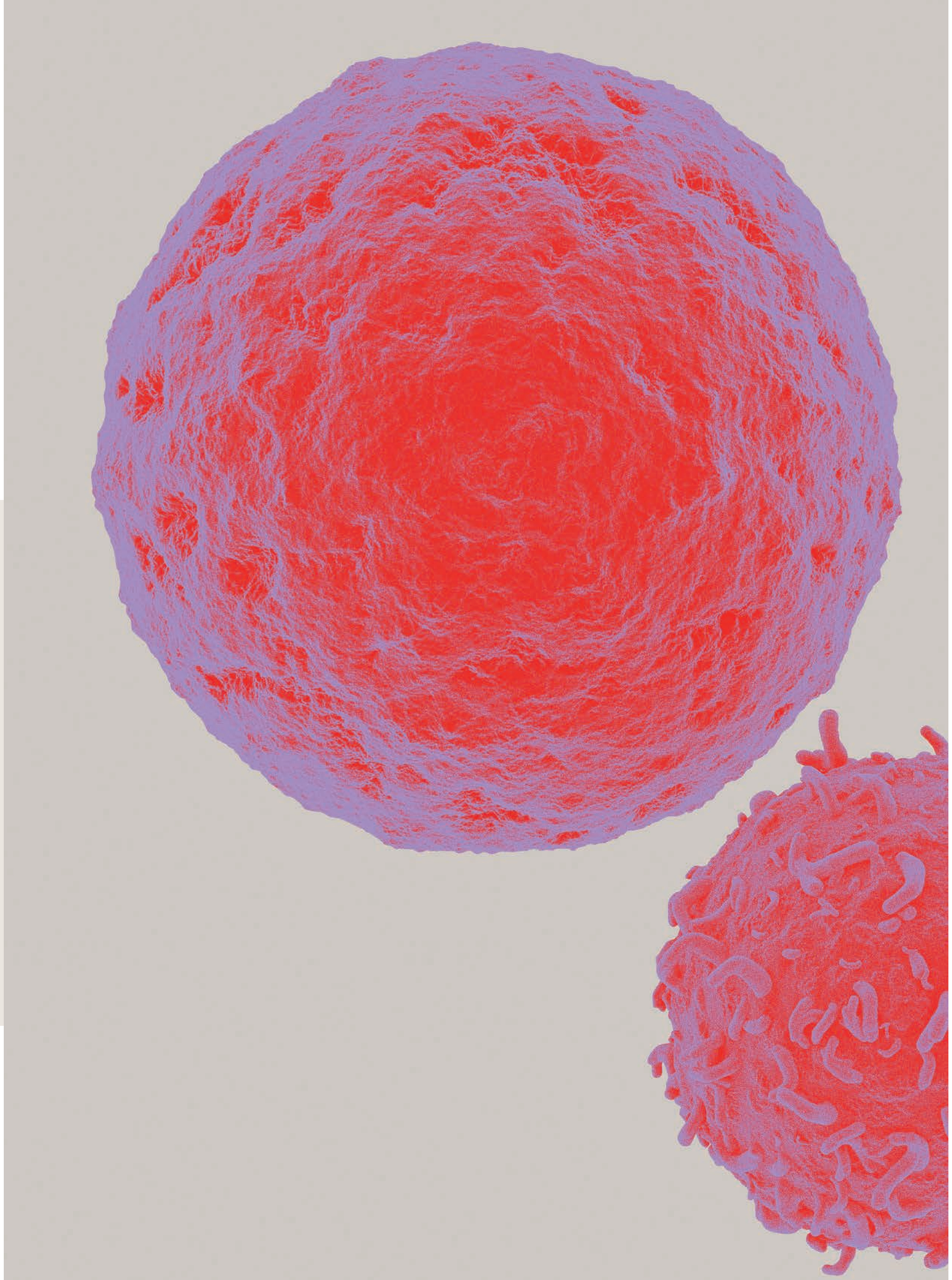
Long-term follow up

Length of follow up period[1]

- Patients should be monitored daily for 14 days after the ciltacabtagene autoleucel infusion at a qualified clinical facility and then periodically for an additional 2 weeks after ciltacabtagene autoleucel infusion for signs and symptoms of CRS, neurologic events and other toxicities.
- Patients should be instructed to remain within proximity of a qualified clinical facility for at least 4 weeks following infusion.

Secondary malignancies including of myeloid and T-cell origin[1]

- Patients treated with ciltacabtagene autoleucel may develop secondary malignancies. T-cell malignancies have been reported following treatment of haematological malignancies with a BCMA- or CD19-directed CAR-T cell therapy, including ciltacabtagene autoleucel. T-cell malignancies, including CAR-positive malignancies, have been reported within weeks and up to several years following administration of a CD19- or BCMA-directed CAR-T cell therapy. There have been fatal outcomes.
- In the event a secondary malignancy occurs, the company should be contacted for reporting and to obtain instructions on patient samples to collect for testing of secondary malignancy of T-cell origin. In patients with HIV infection, contact the company for the testing of secondary malignancies, including those of non-T cell origin.
- Myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML), including cases with fatal outcomes, have occurred in patients after ciltacabtagene autoleucel infusion.
- For more information, please refer to the ciltacabtagene autoleucel Site Accreditation Manuals, which should be available in your department.



1. CARVYKTI 3.2 x 10^6–1.0 x 10^8 cells dispersion for infusion. Saudi Summary of Product Characteristics, January 2025

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Glossary

AML	Acute myeloid leukaemia
ASTCT	American Society for Transplantation and Cellular Therapies
AWB	Airway bill
BCMA	B-cell maturation antigen
CAR	Chimeric antigen receptor
CD	Cluster of differentiation
COI	Chain of identity
CRS	Cytokine release syndrome
CT	Computed tomography
DOB	Date of birth
EBMT-JACIE	European Society for Blood and Bone Marrow Transplantation-Joint Accreditation Committee ISCT-Europe & EBMT
EEG	Electroencephalogram
GBS	Guillain-Barré syndrome
GM-CSF	Granulocyte-macrophage colony-stimulating factor
HCP	Healthcare professional
HLH	Haemophagocytic lymphohistiocytosis
ICANS	Immune effector cell-associated neurotoxicity syndrome
IVIG	Intravenous immunoglobulin
LN2	Liquid nitrogen
MDS	Myelodysplastic syndrome
MNT	Movement and neurocognitive toxicity
MRI	Magnetic resonance imaging
PPE	Personal protective equipment
RMP	Risk management plan
SEC-DIS	Single European code-donation identification sequence

Glossary

SPC	Summary of Product Characteristics
SOP	Standard operating procedure
TOR	Temperature out-of-range

Reporting of adverse events

- Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
- Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.
- In order to improve the traceability of ciltacabtagene autoleucel, the tradename and the batch number of the administered product should be clearly recorded when reporting an adverse event.
- 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.

Adverse events reporting guidance:

- The National Pharmacovigilance Centre (NPC), SFDA:
- Email: npc.drug@sfda.gov.sa
- Telephone: 19999
- Online: http://ade.sfda.gov.sa

For full prescribing information, please refer to the datasheet or contact **Johnson & Johnson Trading Limited (Riyadh)**

- Address: Prince Muhammed Bin Abdulaziz Rd, Tower B, Level 30, Olaya towers.
- Office Tel: 00966-11-4339133
- Postal address: P O Box 65305 Riyadh 11556, Saudi Arabia
- **To report Adverse Events/Product Complaint or any Medical Information Inquiries, please contact us at:**

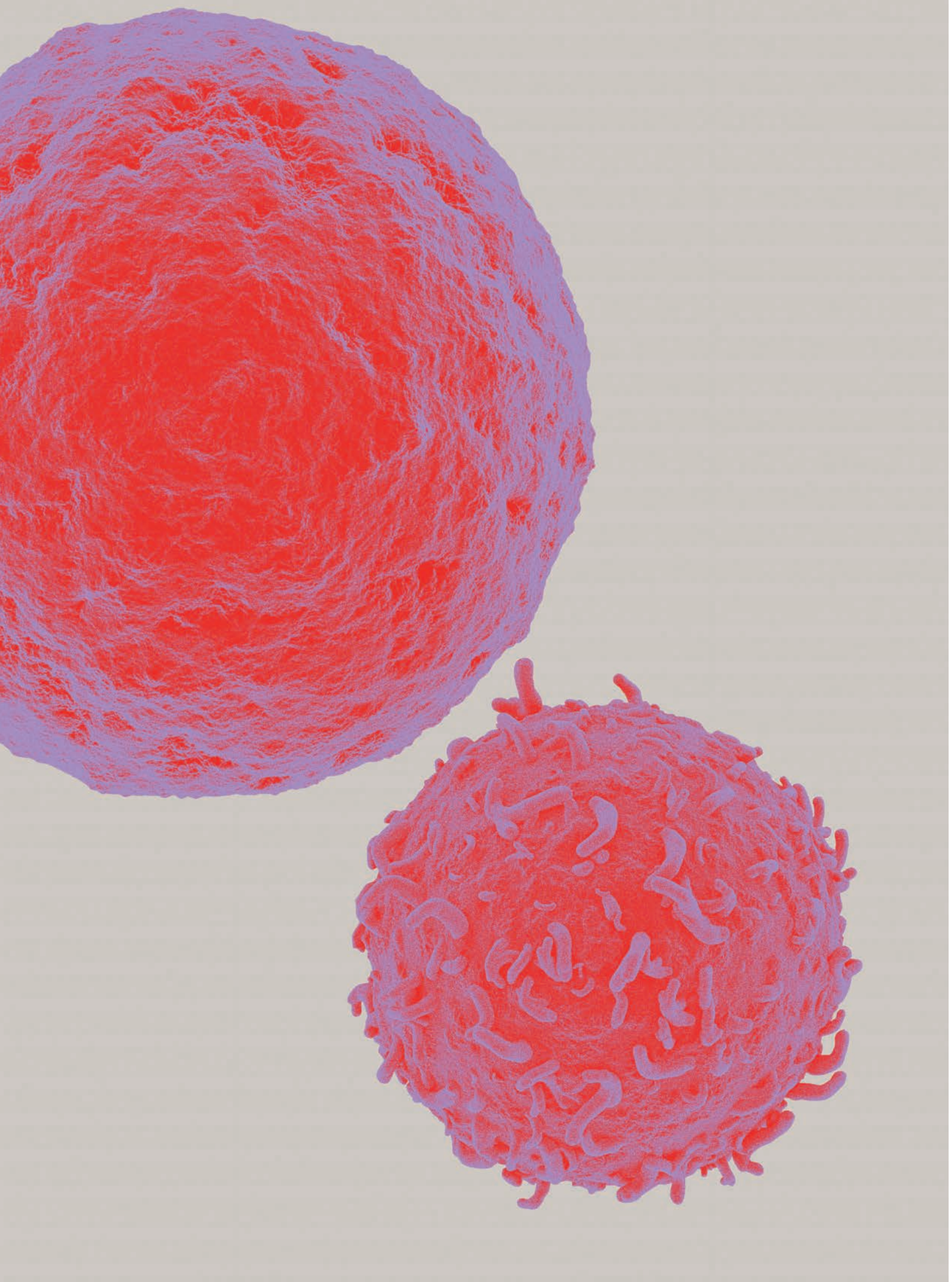
  Email: GCC-PV2@its.jnj.com

  Hotline: 00966540015811

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.

Notes

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.



Adverse events reporting guidance:

- The National Pharmacovigilance Centre (NPC), SFDA:
- Email: npc.drug@sfda.gov.sa
- Telephone: 19999
- Online: http://ade.sfda.gov.sa

For full prescribing information, please refer to the datasheet or contact **Johnson & Johnson Trading Limited (Riyadh)**

- Address: Prince Muhammed Bin Abdulaziz Rd, Tower B, Level 30, Olaya towers.
- Office Tel: 00966-11-4339133
- Postal address: P O Box 65305 Riyadh 11556, Saudi Arabia
- **To report Adverse Events/Product Complaint or any Medical Information Inquiries, please contact us at:**

  Email: GCC-PV2@its.jnj.com

  Hotline: 00966540015811

This guide has been reviewed and approved by The Saudi Food and Drug Authority (SFDA), Version 3, May 2026.