Package leaflet: Information for the patient

CARVYKTI 3.2 × 10^6 – 1 × 10^8 cells dispersion for infusion
ciltacabtagene autoleucel (CAR+ viable T cells)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- The doctor or nurse will give you a Patient Alert Card which contains important safety information about the treatment with CARVYKTI. Read it carefully and follow the instructions on it.
- Carry the Patient Alert Card with you at all times and always show it to any doctor or nurse who sees you or if you go to the hospital.

What is in this leaflet

1. What CARVYKTI is and what it is used for

- CARVYKTI is a type of medicine called a "genetically modified cell therapy" which is made especially for you from your own white blood cells, called T cells.
- CARVYKTI is used to treat adult patients with cancer of the bone marrow called multiple myeloma. It is given when at least one other treatment has not worked.

How CARVYKTI works
- The white blood cells taken from your blood are modified in the laboratory to insert a gene that allows them to make a protein called chimeric antigen receptor (CAR).
- The CAR can attach to a specific protein on the surface of myeloma cells allowing your white blood cells to recognise and attack the myeloma cells.

2. What you need to know before you are given CARVYKTI

You must not be given CARVYKTI
- if you are allergic to any of the ingredients of this medicine (listed in section 6).
- if you are allergic to any of the ingredients in the medicines you will be given to reduce the number of white blood cells in your blood (lymphodepleting therapy) before treatment with CARVYKTI (see also section 3, How CARVYKTI is given).

If you think you may be allergic, ask your doctor for advice.

Warnings and precautions

Patients treated with CARVYKTI may develop new types of cancers. There have been reports of patients developing cancer, beginning in a type of white blood cells called T-cells, after treatment with CARVYKTI and similar medicines. Talk to your doctor if you experience any new swelling of your glands (lymph nodes) or changes in your skin such as new rashes or lumps.

Tell your doctor before you are given CARVYKTI if you have:
- current or past problems with your nervous system - such as fits, stroke, new or worsening memory loss
- any lung, heart or blood pressure (low or raised) problems
- liver or kidney problems.
- signs or symptoms of graft-versus-host disease. This happens when transplanted cells attack your body, causing symptoms such as rash, nausea, vomiting, diarrhoea and bloody stools.

If any of the above apply to you (or you are not sure), talk to your doctor before you are given CARVYKTI.

Tests and checks
Before you are given CARVYKTI your doctor will:
- check the levels of blood cells in your blood
- check your lungs, heart and blood pressure
- look for signs of infection - an infection will be treated before you have CARVYKTI
- check if your cancer is getting worse
- check for hepatitis B, hepatitis C or HIV infection
- check if you had a vaccination in the last 6 weeks or plan to have one in the next few months.

After treatment with CARVYKTI your doctor will:
- regularly check your blood, as the number of blood cells and other blood components may decrease.

Tell your doctor right away if you get a fever, chills or any signs or symptoms of an infection, are feeling tired, or have bruising or bleeding.

Look out for serious side effects
There are serious side effects which you need to tell your doctor or nurse about straight away and which may require you to get immediate medical attention. See section 4 under ‘Serious side effects’.

Children and adolescents
CARVYKTI should not be used in children and adolescents below 18 years of age as the medicine has not been studied in this age group and it is not known if it is safe and effective.

Other medicines and CARVYKTI
Before you are given CARVYKTI tell your doctor or nurse if you are taking, have recently taken, or might take any other medicines.
In particular, tell your doctor or nurse if you are taking:

- medicines that weaken your immune system such as corticosteroids.

These medicines may interfere with the effect of CARVYKTI.

Vaccines and CARVYKTI
You must not be given certain vaccines called live vaccines:
- in the 6 weeks before you are given the short course of chemotherapy (called lymphodepleting chemotherapy) to prepare your body for the CARVYKTI cells.
- after CARVYKTI treatment while your immune system is recovering.

Talk to your doctor if you need to have any vaccinations.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being given this medicine.
- This is because the effects of CARVYKTI in pregnant or breast-feeding women are not known.
- CARVYKTI may harm your unborn baby or your breast-fed child.

If you are pregnant or think you may be pregnant after treatment with CARVYKTI, talk to your doctor immediately.

You have to do a pregnancy test before treatment starts. CARVYKTI should only be given if the results show you are not pregnant.

If you have had CARVYKTI treatment, you should discuss any plans to have future pregnancies with your doctor.

Driving and using tools or machines
CARVYKTI can severely affect your ability to drive or use tools or machines causing side effects that may make you:
- feel tired
- have balance and coordination problems
- feel confused, weak or dizzy.

Do not drive or use tools or machines until at least 8 weeks after having CARVYKTI and if these symptoms return.

CARVYKTI contains dimethylsulfoxide (DMSO) and kanamycin
This medicine contains DMSO (a substance used to preserve frozen cells) and may contain traces of kanamycin (an aminoglycoside antibiotic), both of which can sometimes cause allergic reactions. Your doctor will monitor you for any signs of a possible allergic reaction.

3. How CARVYKTI is given

CARVYKTI will always be given to you by a healthcare professional at a qualified treatment centre.

Making CARVYKTI from your own blood cells
CARVYKTI is made from your own white blood cells. Your blood cells will be collected from you to prepare your medicine.
- Your doctor will take some of your blood using a catheter (tube) placed in your vein.
- Some of your white blood cells are separated from your blood - the rest of your blood is returned to your vein. This process is called ‘leukapheresis’.
- This process can take 3 to 6 hours and may need to be repeated.
- Your white blood cells are sent to the manufacturing centre where they are modified to make CARVYKTI. This process takes about 4 weeks.
- While CARVYKTI is made you may get other medicines to treat the multiple myeloma. This is so it does not get worse.

Medicines given before CARVYKTI treatment

A few days before - you will be given treatment called “lymphodepleting therapy” to prepare your body to receive CARVYKTI. This treatment reduces the number of white blood cells in your blood, so the genetically modified white blood cells in CARVYKTI can grow in numbers when they are returned to your body.

30 to 60 minutes before - you may be given other medicines. These may include:
- Antihistamine medicines for an allergic reaction - such as diphenhydramine
- medicines for fever - such as paracetamol.

Your doctor or nurse will check carefully that the CARVYKTI treatment you are given is from your own white blood cells.

How you are given CARVYKTI
CARVYKTI is a one-time treatment. It will not be given to you again.

- Your doctor or nurse will give you CARVYKTI by a drip into your vein. This is called an 'intravenous infusion' and is usually less than 60 minutes.

CARVYKTI is the genetically modified version of your white blood cells.

- Your healthcare professional handling CARVYKTI will take appropriate precautions to prevent the chance of transfer of infectious diseases.
- They will also follow local guidelines to clean up or dispose of any material that has been in contact with CARVYKTI.

After you are given CARVYKTI
- Plan to stay near the hospital where you were treated for at least 4 weeks after you are given CARVYKTI.
  - You will need to return to the hospital every day for at least 14 days after you are given CARVYKTI. This is so your doctor can check if your treatment is working and treat you if you get any side effects. If you do develop serious side effects, you may need to stay in the hospital until your side effects are under control and it is safe for you to leave.
  - If you miss any appointments, call your doctor or qualified treatment centre as soon as possible to make a new appointment.
- You will be asked to enroll in a registry for at least 15 years in order to monitor your health and better understand the long-term effects of CARVYKTI.
- Having CARVYKTI in your blood may cause some commercial HIV tests to incorrectly give you a HIV positive result even though you may be HIV negative.
- Do not donate blood, organs, tissues or cells for transplants after you have had CARVYKTI.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
CARVYKTI can cause side effects that may be serious or life-threatening.

Serious side effects
Get medical help straight away if you get any of the following serious side effects which may be severe and can be fatal.

- A serious immune reaction known as 'cytokine release syndrome (CRS)', some signs include:

  Very common (may affect more than 1 in 10 people):
  - chills, fever (38°C or higher).
  - fast heart beat, difficulty breathing,
  - low blood pressure which can make you feel dizzy or lightheaded.

- Effects on your nervous system, symptoms of which can occur days or weeks after you receive the infusion, and may initially be subtle. Some of these symptoms may be signs of a serious immune reaction called 'immune effector cell associated neurotoxicity syndrome' (ICANS) or may be signs and symptoms of parkinsonism:

  Very common (may affect more than 1 in 10 people):
  - feeling confused,
  - less alert, disorientated, anxious, memory loss,
  - difficulty speaking or slurred speech,

- slower movements, changes in handwriting

Common (may affect up to 1 in 10 people):
- loss of coordination, affecting movement and balance,
- difficulty reading, writing and understanding words,
- personality changes, which may include being less talkative, disinterest in activities and reduced facial expression

- CARVYKTI may increase the risk of life-threatening infections that may lead to death.

If you notice any of the above side effects, get medical help straight away.

Other side effects
Other side effects are listed below. Tell your doctor or nurse if you get any of these side effects.

Very common (may affect more than 1 in 10 people):
- infected nose, sinuses or throat (a cold)
- bacterial infection
- cough, being short of breath
- pneumonia (lung infection)
- viral infection
- headache
- sleep problems
- pain, including muscle and joint pain
- swelling caused by fluid build up in the body
- feeling very tired
- nausea (feeling sick), decreased appetite, constipation, vomiting, diarrhoea
- problems with movement including muscle spasms, muscle tightness
- nerve damage that may cause tingling, numbness, pain or loss of pain sensation
- low levels of antibodies called immunoglobulins in the blood – which may lead to infections
- low level of oxygen in the blood causing shortness of breath, coughing, headache, and confusion
- increased blood pressure
- bleeding, which can be severe, called a 'haemorrhage'
- abnormal blood tests indicating:
  - low number of white blood cells (including neutrophils and lymphocytes)
  - low levels of 'platelets' (cells that help blood to clot) and red blood cells
  - low levels of calcium, sodium, potassium, magnesium, phosphate in the blood
  - low levels of 'albumin' a type of protein in the blood
  - blood clotting problems
  - increased levels of a protein called 'ferritin' in the blood
  - increased levels of enzymes in the blood called 'gamma-glutamyltransferase' and 'transaminases'

Common (may affect up to 1 in 10 people):
- low number of white blood cells ((neutrophils), which can occur with infection and fever
- gastroenteritis (inflamed stomach and gut)
- stomach pain
- urinary tract infection
- fungal infection
- increased number of a type of white blood cell (lymphocytes)
- severe infection throughout the body (sepsis)
- kidney failure
- abnormal heart beat

- serious immune reaction involving the blood cells - may lead to an enlarged liver and spleen, called ‘haemophagocytic lymphohistiocytosis’
- serious condition where fluid leaks out of the blood vessels into the body tissues called ‘capillary leak syndrome’
- increased levels of enzymes in the blood called ‘alkaline phosphatase’
- muscle tremor
- mild muscle weakness caused by nerve damage
- severe confusion
- facial numbness, difficulty moving muscles of face and eyes
- high level of ‘bilirubin’ in the blood
- blood clot
- skin rash
- increased level of a protein called ‘C-reactive protein’ in the blood that may indicate an infection or inflammation

Uncommon (may affect up to 1 in 100 people):
- tingling, numbness, and pain of hands and feet, difficulty walking, leg and/or arm weakness, and difficulty breathing
- A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin)

Tell your doctor or nurse if you get any of the side effects listed above. Do not try to treat your symptoms with other medicines on your own.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
Yellow Card Scheme
Website: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store CARVYKTI

The following information is intended for doctors only.

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the container label and infusion bag after ‘EXP’.
Store frozen in vapour phase of liquid nitrogen (≤ -120 °C) until thawed for use.
Do not refreeze.

6. Contents of the pack and other information

What CARVYKTI contains
The active substance is ciltacabtagene autoleucel.

Each CARVYKTI infusion bag contains ciltacabtagene autoleucel cell dispersion containing 3.2×10^6 to 1×10^8 CAR-positive viable T cells suspended in a cryopreservative solution.
An infusion bag contains 30 mL or 70 mL of dispersion for infusion.

The other ingredients are a solution (Cryostor CS5) used to preserve frozen cells (see section 2, CARVYKTI contains DMSO and kanamycin).

This medicine contains genetically modified human cells.

What CARVYKTI looks like and contents of the pack
CARVYKTI is a colourless to white, including shades of white, yellow, and pink, 30 ml or 70 ml cell dispersion for infusion, supplied in either a 50 mL or a 250 mL infusion bag respectively, individually packed in an aluminium cryo cassette.

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This leaflet was last revised in July 2024.

The following information is intended for healthcare professionals only:

CARVYKTI should not be irradiated as irradiation could inactivate the medicinal product.

Precautions to be taken before handling or administering the medicinal product
CARVYKTI should be transported within the facility in closed, break-proof and leak-proof containers.

This medicinal product contains human blood cells. Healthcare professionals handling CARVYKTI should take appropriate precautions (wearing gloves, protective clothing and eye protection) to avoid potential transmission of infectious diseases.
CARVYKTI must remain ≤ -120°C at all times, until the content of the bag is thawed for infusion.

Preparation prior to administration
The timing of CARVYKTI 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 CARVYKTI is available for infusion when the patient is ready. Once thawed, the medicinal product should be administered immediately and the infusion should be completed within 2.5 hours.

- Prior to CARVYKTI preparation, patient identity should be confirmed by matching the patient's identity with the patient identifiers on the CARVYKTI cryo cassette and Lot Information Sheet. The CARVYKTI infusion bag should not be removed from the cryo cassette if the information on the patient-specific label does not match the intended patient.
- Once patient identification is confirmed, the CARVYKTI infusion bag should be removed from the cryo cassette.
- The infusion bag should be inspected for any breaches of container integrity such as breaks or cracks before and after thawing. Do not administer if the bag is compromised and contact **Janssen-Cilag Ltd.**

Thawing

- The infusion bag should be placed inside a sealable plastic bag prior to thawing.
- CARVYKTI 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.
- 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. CARVYKTI must not be pre-filtered into a different container, washed, spun down, and/or resuspended in new media prior to infusion.
- Once thawed, the medicinal product should not be re-frozen or refrigerated.

Administration

- CARVYKTI is for autologous single use only.
- Prior to infusion and during the recovery period, ensure tocilizumab and emergency equipment are available for use. In the exceptional case where tocilizumab is not available due to a shortage that is listed in the MHRA Central Alerting System, suitable alternative measures to treat CRS instead of tocilizumab must be available prior to infusion.
- Confirm the patient's identity with the patient identifiers on the CARVYKTI infusion bag and Lot Information Sheet. Do not infuse CARVYKTI if the information on the patient-specific label does not match the intended patient.
- Once thawed, the entire contents of the CARVYKTI 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 min.
- Do NOT use a leukodepleting filter.
- Gently mix the contents of the bag during CARVYKTI infusion to disperse cell clumps.
- 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.

<u>Precautions to be taken for the disposal of the medicinal product</u>

Unused medicinal product and all material that has been in contact with CARVYKTI (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.

<u>Accidental exposure</u>

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 CARVYKTI must be decontaminated with appropriate disinfectant.