Package leaflet: Information for the patient

Yescarta 0.4 – 2 × 10^8 cells dispersion for infusion
axicabtagene ciloleucel (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.
- Your doctor will give you a Patient Alert Card. Read it carefully and follow the instructions on it.
- Always show the Patient Alert Card to the doctor or nurse when you see them or if you go to hospital.
- 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.

What is in this leaflet

1. What Yescarta is and what it is used for

Yescarta is a gene therapy medicine used for treating adults with aggressive diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma (FL) affecting your lymph tissue (part of the immune system) that affects a type of white blood cell called B lymphocytes and other organs in your body. Too many of these abnormal white blood cells accumulate in your tissue and this is the cause of the symptoms you may have.

The medicine is made specially for you as a single administration of your own modified white blood cells.

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

You must not be given Yescarta:
- if you are allergic to axicabtagene ciloleucel or any of the other ingredients of this medicine (listed in section 6).
- if you cannot receive treatment, called lymphodepleting chemotherapy, which reduces the number of white blood cells in your blood (see also section 3, How Yescarta is given).

Warnings and precautions

Yescarta is made from your own white blood cells and must only be given to you (*autologous use*).

Before you are given Yescarta you must tell your doctor if you:
- have problems with your nervous system (such as fits, stroke, or memory loss).
- have kidney problems.

- have low blood cell levels (blood counts).
- have had a stem cell transplant in the last 4 months.
- have any lung, heart or blood pressure (low or raised) problems.
- have 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.
- notice the symptoms of your cancer are getting worse. If you have lymphoma this might include fever, feeling weak, night sweats, sudden weight loss.
- have an infection. The infection will be treated before the Yescarta infusion.
- have had hepatitis B, hepatitis C or human immunodeficiency virus (HIV) infection.

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

Tests and checks
Before you are given Yescarta your doctor will:
- Check your lungs, heart and blood pressure.
- Look for signs of infection; any infection will be treated before you are given Yescarta.
- Check if your cancer is getting worse.
- Look for signs of graft-versus-host disease that can happen after a transplant.
- Check your blood for uric acid and for how many cancer cells there are in your blood. This will show if you are likely to develop a condition called tumour lysis syndrome. You may be given medicines to help prevent the condition.
- Check for hepatitis B, hepatitis C or HIV infection.
- Check if you had a vaccination in the previous 6 weeks or are planning to have one in the next few months.

After you have been given Yescarta
Tell your doctor or nurse immediately if you have any of the following:
- Chills, extreme tiredness, weakness, dizziness, headache, cough, shortness of breath, or rapid heartbeat, which may be symptoms of a condition known as cytokine release syndrome. Take your temperature twice a day for 3-4 weeks after treatment with Yescarta. If your temperature is high, see your doctor immediately.
- Fits, shaking, or difficulty speaking or slurred speech, loss of consciousness or decreased level of consciousness, confusion and disorientation, loss of balance or coordination.
- Fever, which may be a symptom of an infection.
- Extreme tiredness, weakness and shortness of breath, which may be symptoms of a lack of red blood cells.
- Bleeding or bruising more easily, which may be symptoms of low levels of cells in the blood known as platelets.

Your doctor will regularly check your blood counts as the number of blood cells and other blood components may decrease.

Do not donate blood, organs, tissues or cells for transplants.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you are given Yescarta. Your doctor may need to take special care of you during your treatment with Yescarta.

In some cases, it might not be possible to go ahead with the planned treatment with Yescarta. For example:

- If Yescarta infusion is delayed for more than 2 weeks after you have received preparatory chemotherapy you may have to receive more preparative chemotherapy.

Children and adolescents

Yescarta must not be used in children and adolescents below 18 years of age because Yescarta has not been studied in this age group.

Other medicines and Yescarta

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

Before you are given Yescarta tell your doctor or nurse if you are taking any medicines that weaken your immune system such as corticosteroids, since these medicines may interfere with the effect of Yescarta.

In particular, 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 Yescarta cells.
- During Yescarta treatment.
- After treatment while the 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 Yescarta in pregnant or breast-feeding women are not known, and it may harm your unborn baby or your breast-fed child.
- If you are pregnant or think you may be pregnant after treatment with Yescarta, talk to your doctor immediately.
- You will be given a pregnancy test before treatment starts. Yescarta can only be given if the results show you are not pregnant.

Discuss pregnancy with your doctor if you have received Yescarta.

Driving and using machines
Some people may feel tired, dizzy or have some shaking after being given Yescarta. If this happens to you, do not drive or use heavy machines until at least 8 weeks after infusion or until your doctor tells you that you have completely recovered.

Yescarta contains sodium, dimethyl sulphoxide (DMSO), and residual gentamicin
This medicine contains 300 mg sodium (main component of cooking/table salt) in each infusion bag. This is the equivalent to 15% of the recommended maximum daily dietary intake of sodium for an adult.

This medicine contains DMSO and residual gentamicin which may cause severe allergic reactions.

3. How Yescarta is given

Yescarta will always be given to you by a healthcare professional. It is given by a drip (infusion) into a vein (intravenously).

- Since Yescarta is made from your own white blood cells, your cells will be collected from you to prepare your medicine. Your doctor will take some of your blood using a catheter placed in your vein (a procedure call leukapheresis). Some of your white blood cells are separated from your blood and the rest of your blood is returned to your vein. This can take 3 to 6 hours and may need to be repeated.

- Your white blood cells are sent away to make Yescarta. It usually takes about 3 to 4 weeks to receive your Yescarta therapy but the time may vary.

Medicines given before Yescarta treatment
During the 30 to 60 minutes before you are given Yescarta you may be given other medicines. This is to help prevent infusion reactions and fever. These other medicines may include:
- Paracetamol.
- An antihistamine such as diphenhydramine.

Prior to receiving Yescarta, you will be given other medicines such as preparative chemotherapy, which will allow your modified white blood cells in Yescarta to multiply in your body when the medicine is given to you.

Your doctor or nurse will check carefully that this medicine is yours.

How you are given Yescarta

Yescarta will always be given to you by a doctor in a qualified treatment centre.

- Yescarta is given in a single dose.
- Your doctor or nurse will give you a single infusion of Yescarta through a catheter placed into your vein (intravenous infusion) over about 30 minutes.

You must receive Yescarta infusion in a qualified clinical facility and be discharged only when your doctor thinks it is safe for you to go home.
Your doctor may do blood tests to check for side effects.

After you are given Yescarta
- Plan to stay within proximity from the hospital where you were treated for at least 4 weeks after you have been given Yescarta. Your doctor will recommend that you return to the hospital daily for at least 10 days and will consider whether you need to stay at the hospital as an in-patient for the first 10 days after infusion. This is so your doctor can check if your treatment is working and help you if you have any side effects.

If you miss any appointments, call your doctor or the qualified clinical facility as soon as possible to reschedule your appointment.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Yescarta can cause side effects to your immune system that may be serious or life-threatening, and can lead to death.

The following side effects have been reported with Yescarta.

Very common (may affect more than 1 in 10 people)

- Fever, chills, reduced blood pressure which may cause symptoms such as dizziness, lightheadedness, fluid in the lungs, which may be severe and can be fatal (all symptoms of a condition called *cytokine release syndrome*).
- Abnormally low number of white blood cells, which may increase your risk of infection.
- Loss of consciousness or decreased level of consciousness, confusion or memory loss due to disturbances of brain function, involuntary shaking (*tremor*), sudden confusion with agitation, disorientation, hallucination or irritability (*delirium*).

- Decrease in the number of red blood cells (*cells that carry oxygen*): symptoms can include extreme tiredness with a loss of energy.
- Extreme tiredness.
- Low number of cells that help clot the blood (*thrombocytopenia*): symptoms can include excessive or prolonged bleeding or bruising.
- Muscle and joint pain, back pain.
- Fever or chills, which may be signs of an infection.
- Headache.
- High levels of uric acid or sugar (glucose) seen in blood tests.
- Low levels of sodium or phosphate seen in blood tests.
- Nausea, constipation, diarrhoea, abdominal pain, vomiting.
- Decreased appetite.
- Low blood pressure, dizziness.
- Shortness of breath, cough.
- Fast heartbeat.
- Irregular heartbeat (*arrhythmia*).
- Low levels of immunoglobulins seen in blood test, which may lead to infections.
- Build-up of fluids in tissue (*oedema*) which can lead to swelling, weight gain, difficulty in breathing, and decreased output of urine.
- Lack of energy or strength, muscular weakness, difficulty moving, muscle spasm.
- Skin rash or skin problems.
- Difficulty sleeping.
- High blood pressure.
- Increase in liver enzymes seen in blood tests.

Common (may affect up to 1 in 10 people)

- Dry mouth, dehydration, difficulty swallowing.
- Pain in the hands or feet.
- High levels of bilirubin seen in blood tests.
- Low levels of albumin, potassium or calcium seen in blood tests.
- Low oxygen level in blood.
- Failure of the kidneys causing your body to hold onto fluid which can be serious or life threatening.
- Swelling in the limbs, fluid around the lungs (*pleural effusion*).
- Alteration of the blood ability to form clots (*coagulopathy*): symptoms can include excessive or prolonged bleeding or bruising.
- Changes in vision which makes it difficult to see things (*visual impairment*).
- Pain.
- Sudden, unexpected stopping of the heart (cardiac arrest); this is serious and life-threatening.
- Heart failure.
- Blood clots: symptoms can include pain in the chest or upper back, difficulty breathing, coughing up blood or cramping pain, swelling in a single leg, warm and darkened skin around the painful area.
- Fits (*seizures, including seizures that may be prolonged and life-threatening*).
- Inability to move one side of the body.
- Hypersensitivity: symptoms such as rash, hives, itching, swelling and anaphylaxis.
- Mood disorders.
- Nasal inflammation.
- Weakness or inability to move on one side of the body, making it hard to perform everyday activities like eating or dressing.
- Loss of control of body movements.
- Loss of movement in muscles of the face.
- Anxiety.
- Inability to breathe on one’s own (respiratory failure).
- Weight loss.

Uncommon (may affect up to 1 in 100 people)
- Difficulty understanding numbers.
- Breakdown of muscle tissue that leads to the release of muscle fibre into the blood.
- Improper functioning of at least 2 organs (eg, liver, lungs and kidneys) that requires medical treatment and/or procedures to restore normal organ function.
- Swelling of spinal cord which may cause partial or total paralysis of limbs and torso.
- Paralysis of all four limbs.
- Condition of severe systemic inflammation.

Tell your doctor immediately 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 the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard 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 Yescarta

The following information is intented for doctors only.

Do not use this medicine after the expiry date which is stated on the container label and infusion bag.

Store frozen in vapour phase of liquid nitrogen ≤ -150 °C until thawed for use.
Do not refreeze.

6. Contents of the pack and other information

What Yescarta contains

- The active substance is axicabtagene ciloleucel. Each patient-specific single infusion bag contains a dispersion of anti-CD19 CAR T cells in approximately 68 mL for a target dose of 2 × 10^6 anti-CD19 CAR-positive viable T cells/kg.

- The other ingredients (excipients) are: Cryostor CS10 (contains DMSO), sodium chloride, human albumin. See section 2 “Yescarta contains sodium, dimethyl sulphoxide (DMSO), and residual gentamicin”.

This medicine contains genetically modified human blood cells.

What Yescarta looks like and contents of the pack

Yescarta is a clear to opaque, white to red dispersion for infusion, supplied in an infusion bag individually packed in a metal cassette. A single infusion bag contains approximately 68 mL of cell dispersion.

Marketing Authorisation Holder
Gilead Sciences Ltd
280 High Holborn
London
WC1V 7EE
United Kingdom

Manufacturer
Kite Pharma EU B.V.
Tufsteen 1
2132 NT Hoofddorp
The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Gilead Sciences Ltd
Tel: + 44 (0) 8000 113700

This leaflet was last revised in 10/2022

The following information is intended for healthcare professionals only:

It is important that you read the entire content of this procedure prior to administering Yescarta.

Precautions to be taken before handling or administering the medicinal product

Yescarta must be transported within the facility in closed, break-proof, leak-proof containers.

This medicinal product contains human blood cells. Healthcare professionals handling Yescarta must take appropriate precautions (wearing gloves and eye protection) to avoid potential transmission of infectious diseases.

Work surfaces and materials that have potentially been in contact with Yescarta must be decontaminated according to local guidelines on the handling of waste of human-derived materials.

Preparation prior to administration

- Verify that the patient's identity (ID) matches the patient identifiers on the Yescarta cassette.
- The Yescarta product bag must not be removed from the metal cassette if the information on the patient-specific label does not match the intended patient.
- Once the patient's ID is confirmed, remove the Yescarta product bag from the metal cassette.
- Check that the patient information on the metal cassette label matches that on the bag label. Inspect the product bag for any breaches of container integrity before thawing. If the bag is compromised, follow the local guidelines for handling of waste of human-derived material (or immediately contact Kite).

Thawing

- Place the infusion bag inside a second bag.
- Thaw Yescarta at approximately 37 °C using either a water bath or dry thaw method until there is no visible ice in the infusion bag. 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. Yescarta must not be washed, spun down, and/or re-suspended in new medium prior to infusion. Thawing takes approximately 3 to 5 minutes.
- Once thawed, Yescarta is stable at room temperature (20 ˚C – 25 ˚C) for up to 3 hours. However, Yescarta infusion must begin within 30 minutes of thaw completion.

Do NOT use a leukodepleting filter.

Administration

- The medicine must be administered in a qualified treatment centre by a physician(s) with experience in the treatment of haematological malignancies and trained for administration and management of patients treated with Yescarta.
- Ensure that at least 1 dose of tocilizumab per patient and emergency equipment are available prior to infusion and during the recovery period. Hospitals should have access to an additional dose of tocilizumab within 8 hours of each previous dose. In the exceptional case where tocilizumab is not available due to a shortage that is listed in the MHRA Central Alerting System, ensure that suitable alternative measures to treat CRS instead of tocilizumab are available on-site.
- The patient's identity must be matched with the patient identifiers on the infusion bag.
- Yescarta is for autologous use only.
- Yescarta must be administered as an intravenous infusion using latex-free intravenous tubing without a leukocyte depleting filter within 30 minutes by either gravity or a peristaltic pump.
- Gently agitate the bag during Yescarta infusion to prevent cell clumping. All contents of the infusion bag must be infused.

- Sterile sodium chloride 9 mg/mL (0.9%) (0.154 mmol sodium per mL) solution for injection must be used to prime the tubing prior to infusion as well as rinse it afterwards. When the full volume of Yescarta has been infused, the infusion bag must be rinsed with 10 to 30 mL sodium chloride 9 mg/mL (0.9%) solution for injection by back priming to ensure as many cells as possible are infused into the patient.

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

Precautions to be taken for the disposal of the medicinal product
Unused medicinal product and all material that has been in contact with Yescarta (solid and liquid waste) must be handled and disposed of as potentially infectious waste in accordance with local guidelines on the handling of waste of human-derived material.