Patient leaflet in accordance with the Pharmacists' (Products) Regulations - 1986
This medicine is to be supplied by doctor's prescription only

YESCARTA ®
0.4 – 2 x 10^8 cells dispersion for infusion

Active ingredients:
The active substance is axicabtagene ciloleucel. Each patient-specific single infusion bag contains a dispersion of genetically modified anti-CD19 CAR (chimeric antigen receptor) T cells in approximately 68 mL for a target dose of 2 x 10^6 anti-CD19 CAR-positive viable T cells/kg.

Inactive and allergenic substances: see section 6 *"Additional information*".

Read all of this leaflet carefully before you start taking this medicine. This leaflet contains essential information about this medicine. If you have any further questions, ask your healthcare provider team. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

In addition to the patient leaflet, the product YESCARTA has a patient safety card which contains important safety data that you should be aware of, before receiving treatment YESCARTA and following treatment with YESCARTA. You should follow this information. Read the patient safety card and the patient leaflet before treatment initiation. Keep the patient card, you may need to read it again.

1. What is the medicine intended for?

YESCARTA is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy.

Limitation of Use: YESCARTA is not indicated for the treatment of patients with primary or secondary central nervous system lymphoma.

Therapuetic group: Other antineoplastic agents

YESCARTA is a type of medicine called a "genetically modified cell therapy".

YESCARTA is made specially for you as a single administration of your own modified white blood cells. It is given by a drip (*infusion*) into a vein (*intravenously*).

2. Before the treatment

X Do not take this medicine if:
if you are allergic to the active ingredient axicabtagene ciloleucel or to any of the additional ingredients of this medicine (listed in section 6).

! Special warnings relating to the use of this medicine

YESCARTA is made from your own white blood cells and should only be given to you.

Before YESCARTA treatment you should 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 YESCARTA treatment.

After you have been given YESCARTA
Tell your doctor or healthcare provider team 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 (speak (words) indistinctly so that the sounds run into one another), 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.

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

Children and adolescents

YESCARTA should not be used in children and adolescents below 18 years of age.

Tests and checks
Before YESCARTA treatment your doctor will:
- Check your lungs, heart and blood pressure.
- Look for signs of infection; any infection will be treated before YESCARTA treatment.
- 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 infectious disease that affects the liver type B and C (hepatitis B, hepatitis C) or for infection of the human immunodeficiency virus (HIV).

After YESCARTA treatment your doctor will:
- Monitor you for secondary malignancy for your entire life.
- Test your immunoglobulin levels (proteins produced by the immune system).
- Monitor you at the qualified healthcare facility following infusion at least daily for 10 days to check if your treatment is working and help you if you have any side effects. After the first 10 days after infusion you will be monitored at your doctor’s discretion.

Drug-drug Interactions

Before YESCARTA treatment, tell your healthcare provider team if you are taking or have recently taken any other medicines including non-prescription medicines and dietary supplements. Especially if you are taking or have recently taken 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 following time periods:

- 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, breast-feeding and fertility

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. In addition, the effects on male and female fertility have not been evaluated.

- 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 should 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

Don't drive, use heavy machines or participate in activities that require your alertnace. YESCARA has the potential to cause neurologic events, including altered mental status, or seizures during the 8 weeks after the infusion recovered.

Important information regarding the medicine's ingrediants

This medicine contains 300 mg sodium (main component of cooking/table salt) in each infusion. This is the equivalent to 15% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to take the medcine?

YESCARTA will always be given to you by a healthcare professional.

- 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 frozen and 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 treatment 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 treatment, 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 healthcare provider team will check carefully that this medicine is yours.

How you are given YESCARTA treatment

- YESCARTA is a one-time treatment. It will not be given to you again.
- Your healthcare provider team will give you a single infusion of YESCARTA into your vein for approximately 30 minutes.
- YESCARTA is the genetically modified version of your white blood cells. Your healthcare professional handling YESCARTA will therefore take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases and will follow local biosafety guidelines to clean up or dispose of any material that has been in contact with YESCARTA.

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 YESCARTA treatment

- Plan to stay within proximity from the hospital where you were treated for at least 4 weeks after the YESCARTA treatment. 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.

If you have any further questions on the use of this medicine, consult your healthcare provider team.

4. Side effects

Like all medicines, YESCARTA can cause side effects, do not be alarmed by reading the list of side effects. You may not experience any of them.

YESCARTA treatment 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 side effects (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).
- Decrease in the number of red blood cells which may cause you to feel extremely tired.
- Low blood pressure.
- Dizziness.
- Feeling sick, constipation, diarrhoea, pain in the stomach or being sick.
- Headache, depressed level of consciousness, difficulty in speaking, agitation, shaking.
- Decreased number of white blood cells.
- Decreased blood levels of sodium or phosphate.
- Changes in the rhythm or rate of the heartbeat.

- Anxiety.
- Decrease in the number of platelets (thrombocytopenia).
- Infections in the blood caused by bacteria, viruses or other types of infection.
- Shortness of breath, cough.
- Decreased Immunoglobulins.
- High blood pressure.
- Swelling in the limbs, fluid around the lungs (pleural effusion).
- Muscle and joint pain, back pain.
- Extreme tiredness.
- Dehydration.
- Decreased appetite, weight loss.
- Confusion.
- Increased blood levels of liver enzymes.
- Dry mouth.
- Low oxygen level in blood.
- Pain in the hands or feet.

Common side effects (may affect up to 1 in 10 people)

- Difficulty understanding calculation (dyscalculia), memory loss, fits, loss of control of body movements.
- Failure of the kidneys.
- Fluid in the lungs.
- Respiratory tract infection.
- Sudden, unexpected stopping of the heart (cardiac arrest); this is serious and life-threatening.
- Heart failure.
- Muscle spasms.
- Difficulty to swallow.
- Lung oedema caused by leakage of fluids from blood vessels into surrounding tissue. This can lead to a weight gain and difficulty in breathing.
- Decreased levels of calcium.
- Infections caused by fungi.
- Decreased levels of albumin.
- Skin rash.
- Increased levels of bilirubin.
- Signs and symptoms of blood clots.
- Difficulty sleeping.
- Hypersensitivity.
- Nerve pain.
- Prolonged bleeding or bruising.
- Condition of severe systemic inflammation.

Uncommon (may affect up to 1 in 100 people)

- Inflammation and swelling of spinal cord which may cause partial or total paralysis of limbs and torso.

→Tell your healthcare provider team 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 healthcare provider team. This includes any possible side effects not listed in this leaflet.
You can report any side effects to the Ministry of Health using the online form for reporting side effects found on the home page of the Ministry of Health website www.health.gov.il or at the link below: https://sideeffects.health.gov.il

Additionally, you can also report any side effects directly to the Registration Holder via email: DrugSafety.Israel@gilead.com.

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

5. How to store YESCARTA

Prevent poisoning! Keep this medicine as all other medicines out of the sight and reach of children and/or babiesin this way you will prevent poisoning. Do not induce vomiting without a doctor's express instruction

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

Storage condition:
Store frozen in vapour phase of liquid nitrogen ≤ -150°C until thawed for use.
Do not refreeze. The stability of YESCARTA upon completion of thawing is up to 3 hours at room temperature (20˚C to 25°C). However, YESCARTA infusion should begin within 30 minutes of thaw completion and the total YESCARTA infusion time should not exceed 30 minutes.

As this medicine will be given by qualified healthcare professionals, they are responsible for the correct disposal of the product. These measures will help protect the environment. This medicine contains genetically modified human blood cells. Local biosafety guidelines should be followed for unused medicine or waste material.

6. Additional Information

What YESCARTA contains

The active substance is axicabtagene ciloleucel. Each patient-specific single infusion bag contains a dispersion of genetically modified anti-CD19 CAR (chimeric antigen receptor) T cells in approximately 68 mL for a target dose of 2 x 10^6 anti-CD19 CAR-positive viable T cells/kg.
In addition to the active ingredients, the medicine also contains : Cryostor CS10, sodium chloride, human albumin. See section 2 "Important information regarding the medicine's ingredients".

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.

Manufacturer
Kite Pharma Inc.2355 Utah Avenue
El Segundo, CA 90245
USA

Registration Holder
Gilead Sciences Israel Ltd.
4 HaHarash Street
Hod Hasharon
4524075
Israel

Approved in May 2020

The medicine's registration no. in the national register of medicines at the Ministry of Health: 35695

Reference: EU SmPC from January 2020

The following information is intended for healthcare professionals only:

Preparation of YESCARTA

- 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 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 cassette.
- Check that the patient information on the 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 (or immediately contact Kite).
- Place the infusion bag inside a second sterile bag or per local guidelines.
- 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 should not be washed, spun down, and/or re-suspended in new media prior to infusion. Thawing should take approximately 3 to 5 minutes.
- Once thawed, YESCARTA is stable at room temperature (20˚C-25˚C) for up to 3 hours. YESCARTA infusion should begin within 30 minutes of thaw completion and the total YESCARTA infusion time should not exceed 30 minutes.

YESCARTA must not be irradiated. Do NOT use a leukodepleting filter.

All material that has been in contact with YESCARTA (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local biosafety guidelines. Accordingly, healthcare professionals should take appropriate precautions (wearing gloves and glasses) when handling leukapheresis material or YESCARTA to avoid potential transmission of infectious diseases. Work surfaces and material which have potentially been in contact with YESCARTA must be decontaminated with appropriate disinfectant.

This medicine contains genetically modified human blood cells. Any unused medicine or waste material must be disposed of in accordance with local biosafety guidelines.

For simplicity and ease of reading, this leaflet was phrased in the masculine. Nevertheless, the medicine is intended for both sexes.

Reference: EU SmPC from January 2020

EUJAN20ILMAR20