Patient leaflet in accordance with the Pharmacists' (Products) Regulations - 1986

This medicine is to be supplied by doctor's prescription only

Tecartus®
0.4 – 2 × 10^8 cells dispersion for infusion

Active ingredients:

The active substance is brexucabtagene autoleucel (0.4 – 2 × 10^8 cells dispersion for infusion). Each patient-specific single infusion bag contains a dispersion of anti-CD19 CAR (chimeric antigen receptor)-positive viable T cells in approximately 68 mL for a target dose of 2 x 10^6 anti-CD19 CAR-positive viable T cells/kg for mantle cell lymphoma patients and a target dose of 1 × 10^6 anti-CD19 CAR-positive viable T cells/kg for B-cell acute lymphoblastic leukaemia patients.

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

1. What is the medicine intended for?

Tecartus is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after two or more lines of systemic therapy including a Bruton's tyrosine kinase (BTK) inhibitor unless ineligible to BTK inhibitor.

Limitation of use: Tecartus is not indicated for the treatment of patients with active central nervous system lymphoma.

Tecartus is indicated for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL).

Therapeutic group: Other antineoplastic agents

Mantle cell lymphoma and B-cell acute lymphoblastic leukaemia are cancers of a part of the immune system (the body's defences). They affects a type of white blood cell called B-lymphocytes. In both mantle cell lymphoma and B-cell acute lymphoblastic leukaemia, B-lymphocytes grow in an uncontrolled way and build up in the lymph tissue, bone marrow or blood.

How Tecartus works

The white blood cells are taken from your blood and are genetically modified so that they can target the cancer cells in your body. When Tecartus is infused into your blood, the modified white blood cells will kill the cancer cells.

2. Before the treatment

Do not take this medicine if:

- You are allergic to any of the ingredients of this medicine (listed in section 6).
- You can't receive the medicine to reduce the number of white blood cells in your blood (*lymphodepleting chemotherapy*) (see also section 3, How the medicine is given?).

Special warnings related to the use of this medicine

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

Patients treated with Tecartus 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 other 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.

Before you have been given Tecartus, tell your doctor if:

- You had or have disorders of the brain or spinal cord (*central nervous system*).
- You have any lung, heart, kidney or liver problems.

After you have been given Tecartus

Tell your healthcare provider team immediately or get emergency help right away if you have any of the following:

- Chills, extreme tiredness, weakness, dizziness, headache, cough, shortness of breath, rapid or irregular heartbeat, severe nausea, vomiting, or diarrhoea which may be symptoms of a condition known as *cytokine release syndrome.* Take your temperature twice a day for 3 to 4 weeks after treatment with Tecartus. 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 (e.g. temperature above 38°C), 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.

If any of the above apply to you (or you are not sure), talk to your healthcare provider team.

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.

Children and adolescents

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

Tests and checks

Before you are given Tecartus your doctor will:

- Check your lungs, heart, kidney and blood pressure.
- Look for signs of infection or inflammation; and decide whether you need to be treated before you are given Tecartus.
- Check if your cancer is getting worse.

- Look for signs of graft-versus-host disease that can happen after a transplant. This happens when transplanted cells attack your body, causing symptoms such as rash, nausea, vomiting, diarrhoea and bloody stools.
- 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.
- Check if you have previously received a treatment that attaches to the protein called CD19.

In some cases, it might not be possible to go ahead with the planned treatment with Tecartus. If Tecartus infusion is delayed for more than 2 weeks after you have received lymphodepleting chemotherapy you may have to receive more chemotherapy (see also section 3, How the medicine is given?).

Drug-drug interactions

If you are taking or have recently taken any other medicines including non-prescription medicines and dietary supplements tell it to your healthcare provider team. 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 Tecartus.

In particular, you must not be given certain vaccines called live vaccines:
- In the 6 weeks before you are given the short course of lymphodepleting chemotherapy to prepare your body for the Tecartus cells.
- During Tecartus 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 Tecartus 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 in animal studies.
- If you are pregnant or think you may be pregnant after treatment with Tecartus, talk to your doctor immediately.
- You will be given a pregnancy test before treatment starts. Tecartus should only be given if the results show you are not pregnant.

Discuss pregnancy with your doctor if you have received Tecartus.

Driving and using machines

Do not drive, use heavy machines, or take part in activities that need you to be alert for at least 8 weeks after your Tecartus treatment or until your doctor tells you that you have completely recovered. Tecartus has the potential to cause problems such as altered or decreased consciousness, confusion and seizures (fits) for at least 8 weeks after your treatment.

Important information regarding part of the medicine's ingredients

This medicine contains 300 mg sodium (main component of cooking/table salt) in each infusion bag. This is equivalent to 15% of the recommended maximum daily dietary intake of sodium for an adult. It also contains DMSO and gentamicin which may cause severe hypersensitivity reactions.

3. How the medicine is given?

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

- Since Tecartus 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 a manufacturing center to make your Tecartus. It usually takes about 2 to 3 weeks to make Tecartus but the time may vary.

Medicines given before Tecartus treatment

A few days before you receive Tecartus, you will be given lymphodepleting chemotherapy, which will allow the modified white blood cells in Tecartus to multiply in your body when the medicine is given to you.

During the 30 to 60 minutes before you are given Tecartus 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.

How you are given Tecartus

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

- Tecartus is given in a single dose.
- Your healthcare provider team will give you a single infusion of Tecartus through a catheter placed into your vein (*intravenous infusion*) over about 30 minutes.
- Tecartus is the genetically modified version of your white blood cells. Your healthcare professional handling the treatment will therefore take appropriate precautions (wearing gloves and glasses) to avoid potential transmission of infectious diseases and will follow local guidelines on handling of waste of human-derived material to clean up or dispose of any material that has been in contact with it.

After you are given Tecartus

- You must stay close to the hospital where you were treated for at least 4 weeks after Tecartus treatment. Your doctor will recommend that you return to the hospital daily for at least 10 days or that you stay at the hospital as an in-patient for the first 10 days after Tecartus treatment. 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 your treatment centre 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, Tecartus can cause side effects for some of the patients. Do not be alarmed by reading the list of side effects, you may not experience any of them. Do not try to treat your side effects on your own.

Tecartus can cause side effects that may be serious or life-threatening. **Get urgent medical attention** if you get any of the following side effects after the Tecartus infusion.

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*).
- Loss of consciousness or decreased level of consciousness, confusion or memory loss due to disturbances of brain function, difficulty speaking or slurred speech, involuntary shaking (*tremor*), fits (*seizures*), sudden confusion with agitation, disorientation, hallucination or irritability (*delirium*).
- Fever, chills, which may be signs of an infection.

Other possible side effects

Other side effects are listed below. If these side effects become severe or serious, tell your doctor immediately.

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

- Abnormally low number of white blood cells, which may increase your risk of infection.
- Low number of cells that help clot the blood *(thrombocytopenia)*: symptoms can include excessive or prolonged bleeding or bruising.
- High blood pressure.
- Decrease in the number of red blood cells (cells that carry oxygen): symptoms can include extreme tiredness with a loss of energy.
- Extreme tiredness.
- Fast or slow heartbeat.
- Decrease of oxygen reaching body tissues: symptoms can include changes to the colour of your skin, confusion, rapid breathing.
- Shortness of breath, cough.
- Excessive bleeding.
- Nausea, constipation, diarrhoea, abdominal pain, vomiting.
- Muscle pain, joint pain, bone pain, pain in the extremities of the body.
- Lack of energy or strength, muscular weakness, difficulty moving, muscle spasm.
- Headache.
- Kidney problems causing your body to hold onto fluid, build-up of fluids in tissue *(oedema)* which can lead to weight gain and difficulty in breathing.
- High levels of uric acid and sugar *(glucose)* seen in blood tests.
- Low levels of sodium, magnesium, phosphate, potassium or calcium seen in blood tests.
- Decreased appetite, sore mouth.
- Difficulty sleeping, anxiety.
- Swelling in the limbs, fluid around the lungs *(pleural effusion)*.
- Skin rash or skin problems.
- Low levels of immunoglobulins seen in blood test, which may lead to infections.
- Increase in liver enzymes seen in blood tests.
- Nerve pain.

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

- Low levels of albumin seen in blood tests.
- High levels of bilirubin seen in blood tests.
- Irregular heartbeat *(arrhythmia)*.
- Loss of control of body movements.
- Dry mouth, dehydration, difficulty swallowing.
- Decreased output of urine (due to kidney problems described above).
- Breathlessness *(respiratory failure)*.
- Difficulty breathing which makes you unable to speak in full sentence, cough due to fluid in the lungs.
- Increase of the pressure inside your skull.
- 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.
- 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)*.
- Infusion related reactions: symptoms including dizziness or fainting, flushing, rash, itching, fever, shortness of breath or vomiting, abdominal pain, and diarrhoea.
- Hypersensitivity: symptoms such as rash, hives, itching, swelling and anaphylaxis.

A new type of cancer beginning in a type of white blood cells called T-cells (secondary malignancy of T-cell origin) has been reported for other similar medicines.

→ If any of the side effects appeared or worssen, or you suffer from side effects which are not listed in the leaflet, tell your doctor immediately.

Reporting of side effects

You can report any side effects to the Ministry of Health by clicking on the link "reporting side effect effects following medical treatment" found on the home page of the Ministry of Health website (www.health.gov.il) which directs you to the online side effects reporting form or by clicking on the link: https://sideeffects.health.gov.il.

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

5. How to store Tecartus

The following information is intended for doctors only.

Prevent poisoning! Keep this medicine as all other medicines out of the sight and reach of children and/or babies in this way you will prevent poisoning.

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

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

Tecartus is stable at room temperature (20°C to 25°C) for up to 3 hours after thawing. However, Tecartus infusion should begin within 30 minutes of thaw completion and the total infusion time should not exceed 30 minutes.

6. Additional information

What Tecartus contains

The active substance is brexucabtagene autoleucel ($0.4 – 2 \times 10^8$ cells dispersion for infusion). Each patient-specific single infusion bag contains a dispersion of anti-CD19 CAR (chimeric antigen receptor)-positive viable T cells in approximately 68 mL for a target dose of 2×10^6 anti-CD19 CAR-positive viable T cells/kg for mantle cell lymphoma patients and a target dose of 1×10^6 anti-CD19 CAR-positive viable T cells/kg for B-cell acute lymphoblastic leukaemia patients.
The other ingredients (excipients) are: Cryostor CS10 (contains DMSO), sodium chloride, human albumin. See section 2 “Important information regarding the medicine's ingredients”.

This medicine contains genetically modified human blood cells.

What Tecartus looks like and contents of the pack

Tecartus 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 EU Inc.
2355 Utah Avenue
El Segundo, CA 90245
USA

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

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The following information is intended for healthcare professionals only:

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

<u>Precautions to be taken before handling or administering the medicinal product</u>

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

This medicinal product contains human blood cells. Healthcare professionals handling Tecartus 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 Tecartus must be decontaminated according to local guidelines on the handling of waste of human-derived materials.

<u>Preparation prior to administration</u>

- Verify that the patient’s identity (ID) matches the patient identifiers on the Tecartus metal cassette.

- The Tecartus infusion 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 infusion bag from the metal cassette.
- Check that the patient information on the metal cassette label matches that on the bag label.
- Inspect the infusion 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 Tecartus 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. Tecartus must 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, Tecartus is stable at room temperature (20 °C – 25 °C) for up to 3 hours. However, the 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 Tecartus.
- Ensure that at least 1 dose of tocilizumab per patient and emergency equipment are available prior to infusion and during the recovery period. Hospitals and associated centres should have access to an additional dose of tocilizumab within 8 hours of each previous dose.
- The patient's identity should be matched with the patient identifiers on the infusion bag.
- Tecartus is for autologous use only.
- Tecartus should 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 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 should be used to prime the tubing prior to infusion as well as rinse it afterwards. When the full volume of Tecartus has been infused, the infusion bag should 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.

<u>Precautions to be taken for the disposal of the medicinal product</u>
Any unused medicinal product or waste material that has been in contact with Tecartus (solid and liquid waste) must be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling of waste of human-derived material.

Accidental exposure
In case of accidental exposure local guidelines on handling of human-derived material must be followed in case of accidental exposure, which may include washing of the contaminated skin, removal of contaminated clothes. Work surfaces and material which have potentially been in contact with Tecartus must be decontaminated with appropriate disinfectant.

Medicine's registration no. in the national register of medicines at the Ministry of Health: 36655

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

Revised in September 2024 according to MOHs guidelines.
Reference: EU PIL from August 2024

IL-SEP24-EU-AUG24