CONFIDENTIAL

Manufacturing Site 2D Code Area
Local Code Inventory Part Number

Artwork ID Code Area

FRONT SIDE

120.7 | 120.7 | 120.7 | 120.7

320.7

135.7

476.2

320.7

135.7

Perforation Line (if applicable)
Printing Line (if applicable)

95.25 | 114.1

PRO-000975-5

1466888A1

Package leaflet: Information for the patient

Breyanzi 1.1-70 × 10⁶ cells/mL / 1.1-70 × 10⁶ cells/mL dispersion for infusion
lisocabtagene maraleucel
(chimeric antigen receptor [CAR] positive 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 card. Read it carefully and follow the instructions on it.
- Always show the Patient card to the doctor or nurse when you see them or if you go into 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 Breyanzi is and what it is used for
2. What you need to know before you are given Breyanzi
3. How Breyanzi is given
4. Possible side effects
5. How to store Breyanzi
6. Contents of the pack and other information

1. What Breyanzi is and what it is used for

What Breyanzi is
Breyanzi contains the active substance lisocabtagene maraleucel, a type of treatment called 'genetically modified cell therapy'.

Breyanzi is made from your own white blood cells. This involves taking some of your blood and separating out the white blood cells and sending the white blood cells to a laboratory so that they can be modified to make Breyanzi.

What Breyanzi is used for
Breyanzi is used to treat adults with a type of blood cancer called lymphoma which affects your lymph tissue and causes white blood cells to grow out of control. Breyanzi is used for:
- diffuse large B-cell lymphoma
- high-grade B-cell lymphoma
- primary mediastinal large B-cell lymphoma
- follicular lymphoma.
- mantle cell lymphoma

How Breyanzi works
- Breyanzi cells have been genetically modified to recognise the lymphoma cells in your body.
- When these cells are then introduced back into your blood, they can recognise and attack the lymphoma cells.

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

You should not be given Breyanzi:
- if you are allergic to any of the ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice.
- if you cannot receive treatment, called lymphodepleting chemotherapy, which reduce the number of white blood cells in your blood (see also section 3, How Breyanzi is given).

Warnings and precautions
Before you are given Breyanzi you should tell your doctor if:
- you have any lung or heart problems
- you have low blood pressure
- you have an infection or other inflammatory conditions. The infection will be treated before you are given Breyanzi
- you have had a stem cell transplant from another person in the last 4 months – the transplanted cells can attack your body (graft-versus-host disease), causing symptoms such as rash, nausea, vomiting, diarrhoea and bloody stools
- you notice the symptoms of your cancer are getting worse. These symptoms include fever, feeling weak, night sweats, sudden weight loss
- you have had hepatitis B or C, or human immunodeficiency (HIV) infection
- you had a vaccination in the last 6 weeks or you are planning to have one in the next few months. See **Live vaccines** below for more information.

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

Patients treated with Breyanzi 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 Breyanzi 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.

Tests and checks
Before you are given Breyanzi, your doctor will:
- check your lungs, heart and blood pressure
- look for signs of infection – any infection will be treated before you receive Breyanzi
- look for signs of graft-versus-host disease, which can happen after a stem cell transplant from another person
- 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 if your cancer is getting worse
- check for hepatitis B and C, and HIV infection

After you have been given Breyanzi
- If you get certain serious side effects, you must tell your doctor or nurse straight away because you may need treatment for them. See section 4 under 'Serious side effects'.
- Your doctor will regularly check your blood counts, as the number of blood cells may decrease.
- Stay close to the treatment centre where you had Breyanzi for at least 2 weeks. Your doctor may recommend you stay longer to make sure the care you get after your treatment meets your individual needs. See sections 3 and 4.
- Do not donate blood, organs, tissues or cells for transplantation.

You will be asked to enrol in a registry for at least 15 years in order to better understand the long-term effects of Breyanzi.

Children and adolescents
Breyanzi should not be given to children and adolescents below 18 years of age.

Other medicines and Breyanzi
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines including medicines taken without a prescription.
See section 3 for information about the medicines you will be given before having Breyanzi.

Medicines that affect your immune system
Before you are given Breyanzi tell your doctor or nurse if you are taking any medicines that weaken your immune system such as:
- corticosteroids.

This is because these medicines may reduce the effect of Breyanzi.

Other medicines that treat cancer
Some anti-cancer medicines could reduce the effect of Breyanzi. Your doctor will consider if you need other cancer treatments.

Live vaccines
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 Breyanzi.
- during Breyanzi treatment
- after 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 or lymphodepleting chemotherapy. The effects of Breyanzi in pregnant or breast-feeding women are not known, and it may harm your unborn baby or breast-fed child.
- If you are pregnant or think you may be pregnant after treatment with Breyanzi, talk to your doctor immediately.
- You will be given a pregnancy test before treatment starts. Breyanzi should only be given if the result shows you are not pregnant.

Discuss the need for contraception with your doctor.

Discuss pregnancy with your doctor if you have received Breyanzi.

Driving and using machines
Do not drive machines, or take part in activities that need you to be alert for at least 4 weeks after treatment. Breyanzi can make you sleepy, decrease awareness, and cause confusion and seizures (fits). Based on your individual needs, your doctor may advise you to wait longer before driving.

Breyanzi contains sodium, potassium and dimethyl sulfoxide (DMSO)
This medicine contains up to 12.5 mg sodium (main component of cooking/table salt) per vial. This is equivalent to 0.6% of the recommended maximum daily intake of sodium for an adult. Up to 8 vials of this medicine may be given per dose, which in total contains 100 mg sodium or 5% of the recommended maximum daily intake of sodium for an adult.

This medicine contains up to 0.2 mmol (or 6.5 mg) potassium per dose. Your doctor will take this potassium content into consideration if your kidneys do not work properly or you are on a controlled potassium diet.
This medicine also contains DMSO which may cause severe hypersensitivity reactions.

3. How Breyanzi is given

Patient Card
- Your doctor will give you a Patient Card. Read it carefully and follow the instructions on it.
- Always show the Patient Card to the doctor or nurse when you see them or if you go to hospital.

Giving blood to make Breyanzi from your white blood cells

Breyanzi is made from your own white blood cells

- Your doctor will take some of your blood by putting a tube (catheter) in your vein. Some of your white blood cells will be separated from your blood. The rest of your blood is returned to your body. This is called leukapheresis and can take 3 to 6 hours. This process may need to be repeated.
- Your white blood cells will then be sent away to make Breyanzi.

Other medicines you will be given before Breyanzi
- A few days before you receive Breyanzi, you will be given a short course of chemotherapy. This is to clear away your existing white blood cells.
- Shortly before you receive Breyanzi, you will be given paracetamol and an antihistamine medicine. This is to reduce the risk of infusion reactions and fever.

How Breyanzi is given
- Your doctor will check that the Breyanzi was prepared from your own blood by checking that the patient identity information on the medicine labels matches your details.
- Breyanzi is given by infusion (drip) through a tube into a vein.
- You will receive infusions of the CD8 positive cells, followed immediately by infusions of the CD4 positive cells. The time for infusion will vary, but will usually be less than 15 minutes for each of the 2 cell types.

After Breyanzi is given
- Stay close to the treatment centre where you received Breyanzi – for at least 2 weeks.
- During the first week after treatment, you will need to return to the treatment centre 2 to 3 times so that your doctor can check that the treatment is working – and to help you with any side effects. See sections 2 and 4.

If you miss an appointment
Call your doctor or the treatment centre as soon as possible to make another appointment.

4. Possible side effects

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

Serious side effects
Tell your doctor immediately if you get any of the following side effects after being given Breyanzi:

- fever, chills or shaking, feeling tired, fast or uneven heartbeat, feeling light-headed and short of breath – these may be signs of a serious problem called cytokine release syndrome
- confusion, being less alert (decreased consciousness), difficulty speaking or slurred speech, shaking (tremor), feeling anxious, feeling dizzy and headache – these may be symptoms of a condition called immune effector cell-associated neurotoxicity syndrome (ICANS), or signs of problems with your nervous system
- feeling warm, fever, chills or shivering – these may be signs of infection
  The infections may be caused by:
  - low levels of white blood cells, which help fight infections, or
  - low levels of antibodies called immunoglobulins
- blurred vision, loss of vision or double vision, difficulty speaking, weakness or clumsiness of an arm or a leg, a change in the way you walk or problems with your balance, personality changes, changes in thinking, memory and orientation leading to confusion. These may all be symptoms of a serious and potentially fatal brain condition known as progressive multifocal leukoencephalopathy (PML). These symptoms may start several months after treatment has ended and they usually develop slowly and gradually over weeks or months. It is important that your relatives or caregivers are also aware of these symptoms, since they may notice symptoms that you are not aware of.
- feeling very tired, weak and short of breath – these may be signs of low red blood cell levels (anaemia)
- bleeding or bruising more easily –these may be signs of low levels of blood cells known as platelets.

Tell your doctor immediately if you get any of the side effects above after being given Breyanzi, as you may need urgent medical treatment.

Other possible side effects

Very common: may affect more than 1 in 10 people
- difficulty sleeping
- low blood pressure including signs such as dizziness, passing out, or change in eyesight
- cough
- feeling sick or being sick
- diarrhoea or constipation
- stomach pain
- swollen ankles, arms, legs and face
- rash

Common: may affect up to 1 in 10 people
- trouble with balancing or walking
- high blood pressure which may include signs of very bad headaches, sweating or trouble sleeping
- changes in vision
- changes in the way things taste
- numbness and tingling in the feet or hands
- blood clots or problems with blood clotting
- bleeding in your gut
- passing less urine
- infusion reactions – such as feeling dizzy, fever, and shortness of breath
- low blood levels of phosphates
- low levels of oxygen in the blood

Uncommon: may affect up to 1 in 100 people
- a new type of cancer beginning in a type of white blood cells called T cells (secondary malignancy of T cell origin)
- the fast breakdown of cancer cells, resulting in the release of toxic waste products into the bloodstream – a sign may be dark urine with symptoms of nausea or pain on side of stomach
- severe inflammatory condition – symptoms may include fever, rash, enlarged liver, spleen and lymph nodes
- heart weakness, causing shortness of breath and ankle swelling
- fluid around the lungs
- stroke or mini-strokes
- convulsions or seizures (fits)
- weakness of the face muscles, vocal cords or weakness in the body
- swelling of the brain.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist 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 Breyanzi

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 cartons and vial label after 'EXP'.

Store frozen in the vapour phase of liquid nitrogen (≤ -130 °C).

6. Contents of the pack and other information

What Breyanzi contains
- The active substance is lisocabtagene maraleucel. Each 4.6 mL vial contains a dispersion of CAR-positive viable T-cells (CD8 positive cell component or CD4 positive cell component) with a strength of 1.1 × 10^6 to 70 × 10^6 CAR positive viable T cells/mL for each cell component. There may be up to 4 vials of each of the CD8 positive or CD4 positive cell components, depending upon the concentration of cryopreserved medicine.
- The other ingredients (excipients) are Cryostor CS10 (contains dimethyl sulfoxide or DMSO), sodium chloride, sodium gluconate, sodium acetate trihydrate, potassium chloride, magnesium chloride, human albumin, N-acetyl-DL-tryptophan, caprylic acid, water for injections. See section 2, "Breyanzi contains sodium, potassium and dimethyl sulfoxide (DMSO)".

This medicine contains genetically modified human blood cells.

What Breyanzi looks like and contents of the pack
Breyanzi is a cell dispersion for infusion. It is supplied as vials of slightly opaque to opaque, colourless to yellow, or brownish-yellow dispersion. Each vial contains 4.6 mL cell dispersion of either CD8 positive or CD4 positive cell component.

Marketing Authorisation Holder

Bristol-Myers Squibb Pharma EEIG
Plaza 254
Blanchardstown Corporate Park 2
Dublin 15, D15 T867
Ireland

The following information is intended for healthcare professionals only:

Precautions to be taken before handling or administering the medicinal product

Breyanzi must be transported within the treatment centre in the shipper in which it was received.

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

Preparation prior to administration

***Before** thawing the vials*
- Confirm the patient's identity with the patient identifiers on the shipper.
- Breyanzi is composed of CAR+ positive viable T-cells (CD8+ and CD4+ cell components) and CAR- T-cells. Therefore, there is a separate release for infusion certificate (RRC) for each cell component that is shipped. For information on the number of syringes you will receive, refer to the release for infusion certificate (RRC). For CD4+ cell components (syringe labels are provided with the vials).
- Confirm the infusion time in advance and adjust the start time of Breyanzi thaw such that it will be available for infusion within the infusion window.

Note: Once the vials of CAR-positive viable T-cells (CD8+ and CD4+ cell components) are removed from frozen storage, they must be thawed for completion and the cells administered within 2 hours.

Thawing the vials
- Confirm the patient's identity with the patient identifiers on the cell component cartons and the vials(s) to be thawed (RRC).
- Remove the CD8+ cell component carton and CD4+ cell component carton from the outer carton.
- Visually inspect the cell component and the vial(s) for damage. If the vials are damaged, contact the company. Quarantine the damaged vials and return them in the original protective foamer pad, and thaw at room temperature. Thaw all vials at the same time. **Take care to keep the CD8+ and CD4+ cell components separate.**

Dose preparation
- Based on the concentration of CAR-positive viable T-cells for each cell component (as indicated on the vial) for the CD8+ and CD4+ cell components may be required to administer the prescribed dose. Certificates are provided for each CD8+ or CD4+ cell component vial received.

Note: The volume to be drawn up and infused may differ for each component.

- Each 5 mL vial contains a total extractable volume of 4.6 mL of cell dispersion (see Certificate of Release (CofR) Certificates for each component indicates the volume (mL) of each vial to be withdrawn (1 mL, 2 mL, 3 mL or 4 mL). Luer-lock tip syringes (10 mL, 20 mL) to draw up the specified volume from each vial. A 5 mL syringe should not be used to withdraw volumes from the vials.
- **Prepare the syringe(s) of the CD8+ cell component**
  Remove the CD8+ cell component syringe labels and affix the cell component syringe labels to the syringe(s) prior to pulling the cell component into the syringe.
  Repeat the process for the CD4+ cell component.

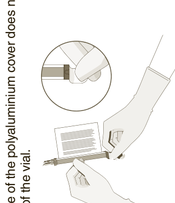
Note: It is important to confirm that the volume drawn up for each cell component matches the volume specified in the cell component certificate for each vial.

Withdrawal of the required volume of cells from each vial into a separate syringe should be carried out using the following instructions:

1. Hold the thawed vial(s) upright and gently invert the vial(s) 8 to 10 times to mix the cells. Do not shake the vial(s). Continue to invert the vial(s) until clumps have dispersed and cells appear to be evenly resuspended.

2. Visually inspect the thawed vial(s) for damage or leaks. Do not use if the vial is damaged or if the clumps do not disperse/ contact the company. The liquid in the vials should be clear to cloudy and colourless to yellow, or brownish-yellow.
3. Remove the polyaluminium cover (if present) from the vial(s) and disinfect the rubber stopper with an alcohol wipe. Allow to air dry before proceeding.

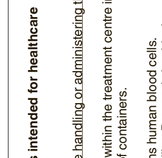
   NOTE: The absence of the polyaluminium cover does not impact the identity of the vial.



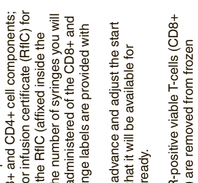
4. Keeping the vial(s) upright, cut the seal on the tubing line on the top of the vial immediately above the filter to open the vial(s) for withdrawal.

   NOTE: Be careful to select the correct tubing line with the filter. Cut ONLY the tubing with a filter.

5. Hold a 20 gauge, 1-1 ½ inch needle, with the opening of the needle tip away from the retrieval port septa, at a 45° angle to puncture the retrieval port septa.
   a. Puncture the retrieval port septa at a 45° angle to the vial's surface and push the needle gradually until the needle enters the vial.
   b. Continue to push the needle gradually until the needle enters the vial.



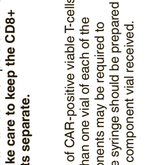
6. WITHOUT drawing air into the syringe, slowly withdraw the required volume of cells as indicated in the release for infusion certificate (RRC).



7. Carefully inspect the syringe for signs of clabins prior to processing. If there is clabrix, contact the company.
8. Verify that the volume of CD8+/CD4+ cell component withdrawn matches the volume specified for each component in the release for infusion certificates (RRC).

   Once the volume is verified, shift the vial and syringe to a horizontal position, and remove the syringe/needle from the vial.

   Carefully detach the needle from the syringe and cap the syringe.



9. Continue to keep the vial horizontal and return it to the carton to avoid leaking from the vial.
10. Dispose of any unused portion of Breyanzi.

Administration

- **Do NOT** use a leukodepleting filter.
- Establish access and ensure adequate venous outgrowth are available before cell dose delivery to minimize the recovery period. In the exceptional case where bridging therapy is not available due to rapid disease progression, the Vein Viability Scoring (VVS) System, ensure that suitable alternative measures to treat infusion reactions are available before the start of infusion.
- Confirm the patient's identity matches the patient identifiers on the syringe label supplied on the respective RPI certificate.
- Once Breyanzi has been drawn into syringes, proceed with administration without delay. Do not refreeze. Do not re-use removal of Breyanzi from frozen storage to patient administration must be completed within 30 minutes.
- Use intravenous sodium chloride 9 mg/mL (0.9%) solution to flush the tubing with each CD8+ cell component administered intravenously at an infusion rate of approximately 10 mL/minute. Flush the tubing with sodium chloride 9 mg/mL (0.9%) after each CD8+ or CD4+ cell component administration.
- Administer each CD8+ cell component immediately after the volume of the CD8+ cell component is completed. Following administration of the CD8+ cell component, flush the tubing with sodium chloride 9 mg/mL (0.9%) solution for injection, using the same infusion rate as the cell component delivered by catheter. The time for infusion will vary and will usually be less than 15 minutes for each component.

Measures to take in case of accidental exposure

In case of accidental exposure local guidelines on handling of biohazardous materials should be followed. Any spillages and materials which have potentially been in contact with the product should 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 it should be disposed of as potentially infectious waste in accordance with local guidelines on handling human-derived material.

Perforation Line (if applicable)
Printing Line (if applicable)

95.25 | 114.1

BACK SIDE

120.7 | 120.7 | 120.7 | 120.7

320.7

135.7

476.2

320.7

135.7

Manufacturer(s)
BMS Netherlands Operations B.V.
Francois Aragostraat 2
2342 DK Oegstgeest
Netherlands

This leaflet was last revised in 04/2026

No Content Area

482.8

Approved v11.0