PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S4**

BENDAMUSTINE 25 mg FRESENIUS

BENDAMUSTINE 100 mg FRESENIUS

Powder for concentrate for solution for infusion

Read all of this leaflet carefully before you receive BENDAMUSTINE FRESENIUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What BENDAMUSTINE FRESENIUS is and what it is used for

BENDAMUSTINE FRESENIUS is a medicine which is used for the treatment of certain types of cancer (cytostatic medicine).

BENDAMUSTINE FRESENIUS is used alone (monotherapy) or in combination with other medicines for the treatment of the following forms of cancer:

- chronic lymphocytic leukaemia
- non-Hodgkin lymphoma which was not treated before, in combination treatment with rituximab or which had not, or only shortly, responded to prior ritumixab treatment (monotherapy)
- multiple myeloma

2. What you need to know before you are given BENDAMUSTINE FRESENIUS

BENDAMUSTINE FRESENIUS should not be administered to you:

- if you are hypersensitive (allergic) to bendamustine or to mannitol.
- during pregnancy, or if you are breastfeeding your baby.
- if you have severe liver damage (damage to the functional cells of the liver).
- if you have yellowing of the skin or whites of the eyes caused by liver or blood problems (jaundice).
- if you have weakened bone marrow function (bone marrow depression) and serious changes in the number of white blood cells and platelets in your blood (determined by blood tests conducted by your doctor).
- if you have had major surgical operations less than 30 days before starting treatment.
- if you have an infection, especially one accompanied by a reduction in white blood cells (leukopenia).
- in combination with yellow fever vaccines or other live (attenuated) vaccines.
- if you have QT prolongation (heart rhythm condition that can potentially cause fast, chaotic heartbeats).

Warnings and precautions

Only experienced doctor or healthcare provider in cancer chemotherapy should provide you with treatment.

Tell your doctor or healthcare provider before being given the injection:

Take special care with BENDAMUSTINE FRESENIUS:

- if you have a reduced capability of the bone marrow to replace blood cells. You should have your full blood count checked before starting treatment with BENDAMUSTINE FRESENIUS, before each subsequent course of treatment and in the intervals between courses of treatment.
- if you have any existing infections, which may also include TB (tuberculosis). You should contact your doctor if you have signs of infection, including fever or lung symptoms.
- if you had Hepatitis B or think you may have hepatitis B (determined by tests conducted by your doctor).

- if you get reactions on your skin during treatment with BENDAMUSTINE FRESENIUS. Some of these reactions can be life threatening. If these reactions increase in severity example severe and painful blistering or peeling of the skin, inform your doctor immediately.
- if you have an existing heart disease (e.g. heart attack, chest pain, severely disturbed heart rhythms). **Your doctor will monitor you more closely.**
- if you notice pain in your side, blood in your urine or a reduced amount of urine. When your disease is very severe, your body may not be able to clear all the waste products from the dying cancer cells. This is called tumour lysis syndrome and can cause kidney failure and heart problems within 48 hours of the first dose of BENDAMUSTINE FRESENIUS. Your doctor may ensure that you are adequately hydrated and give you medicines to help prevent it.
- if you get severe allergic or hypersensitivity reactions. You should pay attention to infusion reactions after your first cycle of therapy, with symptoms such as fever, chills, itching and rash. **Inform your doctor immediately.**
- women should not become pregnant during treatment (see Pregnancy, breastfeeding and fertility).
- if you are a man receiving treatment with BENDAMUSTINE FRESENIUS you should not father a child during your treatment and for up to 3 months afterwards. Before starting treatment, you should seek advice on storing your sperm cells because of the possibility of permanent infertility (see Pregnancy, breastfeeding and fertility).
- unintentional injection into the tissue outside blood vessels (extravasal injection) may cause local tissue damage. Your doctor will treat this.

Children

BENDAMUSTINE FRESENIUS has not been used in children.

Other medicines and BENDAMUSTINE FRESENIUS:

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

If BENDAMUSTINE FRESENIUS is used in combination with medicines which inhibit the formation of blood in the bone marrow, the effect on the bone marrow intensified.

If BENDAMUSTINE FRESENIUS is used in combination with medicines which alter your immune response, e.g. ciclosporin and tacrolimus, this effect may be intensified.

Medicines such as BENDAMUSTINE FRESENIUS (cytostatic medicines) may diminish the effectiveness of live-virus vaccination. Additionally cytostatic medicines increase the risk of an infection after vaccination with live vaccines (e.g. viral vaccination).

If BENDAMUSTINE FRESENIUS is used in combination with medicines such as fluvoxamine (antidepressant), ciprofloxacin (used to treat bacterial infections), acyclovir (used to treat virus infections) and cimetidine (used to treat heartburn and stomach ulcers), these medicines can interfere with each other.

BENDAMUSTINE FRESENIUS with food, drink and alcohol

None known.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.

Pregnancy

You should not use BENDAMUSTINE FRESENIUS if you are pregnant. If you are a woman of childbearing potential, you must use an effective method of contraception during treatment and for 6 months after the last dose of BENDAMUSTINE FRESENIUS. If you become pregnant during your treatment with BENDAMUSTINE FRESENIUS, you must immediately inform your doctor and should get genetic consultation.

Fertility

If you are a man, you should not father a child during treatment with BENDAMUSTINE FRESENIUS and for up to 3 months after treatment has stopped. There is a risk that treatment with BENDAMUSTINE FRESENIUS will lead to infertility, and you may seek advice on conservation of your sperm cells before your treatment begins.

Breastfeeding:

BENDAMUSTINE FRESENIUS must not be administered if you are breastfeeding your baby. If treatment with BENDAMUSTINE FRESENIUS is necessary, you must stop breastfeeding your baby until your treatment has been completed.

Driving and using machines

BENDAMUSTINE FRESENIUS has major influence on the ability to drive and use machines (such as dizziness and lack of co-ordination). Patients should not engage in the above activities if they have these symptoms.

3. How BENDAMUSTINE FRESENIUS is given to you

Do not share medicines prescribed for you with any other person.

You will not be expected to give yourself BENDAMUSTINE FRESENIUS. It will be given to you by a person who is qualified to do so. Your doctor will decide exactly how much medicine to give you.

BENDAMUSTINE FRESENIUS is administered into a vein over 30 - 60 minutes either alone (monotherapy) or in combination with other medicines.

There is no time limit laid down as a general rule for treatment with response to BENDAMUSTINE FRESENIUS. Duration of treatment depends on your disease and your treatment.

If you use more BENDAMUSTINE FRESENIUS than you should

Since a healthcare provider will administer BENDAMUSTINE FRESENIUS, he / she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to use BENDAMUSTINE FRESENIUS

Since a healthcare provider will administer BENDAMUSTINE FRESENIUS, it is unlikely that the dose will be missed.

4. Possible side effects

BENDAMUSTINE FRESENIUS can have side effects.

Not all side effects reported for BENDAMUSTINE FRESENIUS are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking BENDAMUSTINE FRESENIUS, please consult your healthcare provider for advice.

If any of the following happens, stop using BENDAMUSTINE FRESENIUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

- An allergic reaction such as sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body), and you may feel you are going to faint.
- Severe skin reactions with ulcers or blisters or peeling of the skin (Steven Johnson Syndrome).

These are all very serious side effects. If you have them, you may have had a serious reaction to BENDAMUSTINE FRESENIUS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Rapid decrease in blood pressure, chest pain, irregular and often rapid heart rate (atrial fibrillation), signs of infection such as fever or chills.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Headache
- Feeling sick (nausea); vomiting
- Mucosal inflammation; fatigue; fever
- Insomnia; dizziness
- Diarrhoea; constipation, stomatitis (sore mouth)
- Hair loss; skin changes; itchy rash (urticaria)
- Missed periods (amenorrhoea)
- Pain; chills; loss of appetite and dehydration
- Infection NOS* (NOS = Not otherwise specified), including opportunistic infection (including Herpes zoster, cytomegalovirus, hepatitis B), an infection caused by fungus (pneumocystis jirovecii pneumonia)
- A group of disorders caused by poorly formed blood cells (myelodysplastic syndrome), acute myeloid leukemia
- Bleeding (haemorrhage), reduction in red blood cells which can make the skin pale and cause weakness or breathlessness (anaemia), neutropenia (a common type of white blood cell important to fighting off infection)
- Hypersensitivity NOS*(NOS = Not otherwise specified)
- Tumour lysis syndrome (a group of metabolic abnormalities that can occur as a complication during the treatment of cancer)
- Cardiac dysfunction, such as palpitations, a condition marked by severe pain in the chest, often also spreading to the shoulders, arms, and neck, owing to an inadequate blood supply to the heart (angina pectoris), disturbed heart rhythms (dysrhythmia)
- Accumulation of fluid in the heart sac (escape of fluid into the pericardial space); heart attack, chest pain (myocardial infarction); heart failure
- Disturbed function (pulmonary dysfunction) of the lungs, low or high blood pressure (hypotension or hypertension)
- Decrease haemoglobin (decrease in the red pigment of the blood), increase creatinine (a chemical waste product that is produced by your muscles), increase blood level of urea (a chemical waste product)

- A rise in liver enzymes AST/ALT {which may indicate inflammation or damage to cells in the liver); a rise in the enzyme alkaline phosphatase (an enzyme made mostly in the liver and bones); a rise in bile pigment (a substance made during the normal breakdown of red blood cells); low potassium blood levels (a nutrient that is necessary for the function of nerve and muscle cells, including those in your heart).

Less frequent side effects:

- Infection of the blood (sepsis), tuberculosis
- Reduction in your bone marrow function, which may make you feel unwell or show up in your blood tests (bone marrow failure), deficiency of all three cellular components of the blood (red cells, white cells, and platelets) (pancytopenia), the rupture or destruction of red blood cells (haemolysis)
- Rapid decrease in blood pressure sometimes with skin reactions or rash (anaphylactic shock) Severe allergic hypersensitivity reactions (anaphylactic reactions); signs similar to anaphylactic reactions (anaphylactoid reactions)
- Disturbed sense of taste; altered sensations (paraesthesia); malaise and pain in the limbs (peripheral neuropathy); serious condition resulting in the blockade of specific receptor in the nervous systems; disorders of the nervous system; lack of coordination (ataxia); inflammation of the brain (encephalitis)
- Irregular and often rapid heart rate (atrial fibrillation)
- Inflammation of the veins (phlebitis), pulmonary fibrosis, inflammation of the air sacs in the lungs (pneumonitis), lung bleeding (pulmonary alveolar haemorrhage)
- Infertility, liver (hepatic) failure, Multi Organ Failure
- Bleeding inflammation of the gullet (haemorrhagic oesophagitis), bleeding of the stomach or gut (gastrointestinal haemorrhage)
- Drowsiness; loss of voice (aphonia)
- Reddening of the skin (erythema); inflammation of the skin (dermatitis); itching (pruritus); skin rash (macular exanthema); excessive sweating (hyperhidrosis)
- Disturbed sense of taste; altered sensations (paraesthesia)
- Increased heart rate (tachycardia)

Not known (frequency cannot be estimated from the available data)

- Excessive urination, including at night, and excessive thirst even after drinking fluids (nephrogenic diabetes insipidus).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of BENDAMUSTINE FRESENIUS.

Patients are asked to report any suspected adverse drug reactions to their healthcare provider or Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

5. How to store BENDAMUSTINE FRESENIUS

Store all medicines out of reach of children.

- Unopened vial: Store at or below 25 °C.
- Keep container in outer container to protect from light

6. Contents of the pack and other information

What BENDAMUSTINE FRESENIUS contains

- The active substance is bendamustine hydrochloride.

  BENDAMUSTINE 25 mg FRESENIUS: One vial contains 25 mg bendamustine hydrochloride.

  BENDAMUSTINE 100 mg FRESENIUS: One vial contains 100 mg bendamustine hydrochloride.

  After reconstitution, the concentrate contains 2,5 mg bendamustine hydrochloride/mL.

- The other ingredient is mannitol.

What BENDAMUSTINE FRESENIUS looks like and contents of the pack

BENDAMUSTINE FRESENIUS is a white to off-white lyophilised powder or cake in vials with rubber closures and flip off seal.

BENDAMUSTINE 25 mg FRESENIUS: amber, tubular glass vials of 20 mL.

BENDAMUSTINE 100 mg FRESENIUS: amber, tubular glass vials of 50 mL.

Holder of Certificate of Registration

Fresenius Kabi South Africa (Pty) Limited

Stand 7, Growthpoint Business Park

162 Tonetti Street

Halfway House, Extension 7

Midrand, 1685

Gauteng

South Africa

Telephone number: +27 (0)11 545 0000

This leaflet was last revised in

10 March 2025

Registration numbers

BENDAMUSTINE 25 mg FRESENIUS: 50/26/0675

BENDAMUSTINE 100 mg FRESENIUS: 50/26/0676

Access to the corresponding Professional Information

The professional information will be printed and packaged with the product.