PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

BEDURAS 25 mg powder for concentrate for solution for infusion

Contains sugar (42,5 mg mannitol per vial).

BEDURAS 100 mg powder for concentrate for solution for infusion

Contains sugar (170 mg mannitol per vial).

Bendamustine hydrochloride

Read all of this leaflet carefully before you receive BEDURAS.

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

What is in this leaflet

1. What BEDURAS is and what it is used for

The active substance is bendamustine hydrochloride.

BEDURAS is used for the treatment of certain types of cancer (cytostatic medicine).

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

- chronic lymphocytic leukaemia, in cases where fludarabine combination chemotherapy is not

appropriate for you

- non-Hodgkin lymphoma, which was not treated before, in combination treatment with rituximab or which had not, or only shortly, responded to prior rituximab treatment (monotherapy)
- multiple myeloma in cases where thalidomide or bortezomib containing therapy is not appropriate for you.

2. What you need to know before you receive BEDURAS

You should not receive BEDURAS:

- if you are hypersensitive (allergic) to bendamustine hydrochloride or any of the other ingredients of BEDURAS (listed in section 6)
- if you are pregnant or breastfeeding your child
- if you have liver function impairment or yellowing of your skin and eyes (also called jaundice)
- if you have severe bone marrow suppression affecting your blood cell count
- 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 a heart rhythm condition or are taking medicines that can potentially cause fast, irregular heartbeats.

Warnings and precautions

Special care should be taken with BEDURAS:

- in case of reduced capability of the bone marrow to replace blood cells.
  You should have your number of white blood cells and platelets in the blood checked before starting treatment with bendamustine, before each subsequent course of treatment and in the intervals between courses of treatment.
- in case of infections. You should contact your doctor if you have signs of infection, including

fever or lung symptoms.

- in case of a history of hepatitis B infection. You should be tested for hepatitis B virus (HPV) before receiving BEDURAS.
- in case of reactions on your skin during treatment with bendamustine. The skin reactions may increase in severity.
- in case of painful red or purplish rash that spreads and blisters and/or other lesions begin to appear in the mucous membrane (e.g. mouth and lips), in particular if you had before light sensitivity, infections of the respiratory system (e.g. bronchitis) and/or fever.
- in cases of existing heart disease (e.g. heart attack, chest pain, severely disturbed heart rhythms).
- in case you notice any pain in your side, blood in your urine or 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. Your doctor may ensure you are adequately hydrated and give you other medicines to help prevent it.
- in case of severe allergic or hypersensitivity reactions. You should pay attention to infusion reactions after your first cycle of therapy.
- if you notice or someone notices in you at any time during or after your treatment any of the following: memory loss, trouble thinking, difficulty walking or sight loss, tell your doctor immediately. These may be due to a very rare but serious brain infection which can be fatal (progressive multifocal leukoencephalopathy or PML).
- if you notice any suspicious skin changes, contact your doctor, because there may be an increased risk of certain types of skin cancer (non-melanoma skin cancer) with the use of BEDURAS.

Other medicines and BEDURAS

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.) If BEDURAS is used in combination with the following, it

may cause an interaction:

- medicines which inhibit the formation of blood in the bone marrow, the effect on the bone marrow may be intensified
- medicines which alter your immune response, this effect may be intensified
- cytostatic medicines may diminish the effectiveness of live-virus vaccination and may increase the risk of an infection after vaccination with live vaccines (e.g. viral vaccination)
- medicine used to treat obsessive-compulsive disorders (e.g. fluvoxamine)
- medicine used to treat certain bacterial infections (e.g. ciprofloxacin)
- medicine used to treat certain viral infections (e.g. aciclovir)
- medicine used to treat heartburn (e.g. cimetidine).

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 health care provider for advice before receiving BEDURAS.

Pregnancy

Bendamustine, as in BEDURAS, can cause genetic damage and has caused malformations in animal studies. You should not receive BEDURAS during pregnancy.

Breastfeeding

Bendamustine, as in BEDURAS, should not be administered during breastfeeding. If treatment with bendamustine is necessary, you must stop breastfeeding your baby until your treatment with BEDURAS has been completed.

Fertility

If you are a woman of childbearing potential you must use an effective method of contraception both before and during treatment with BEDURAS. If pregnancy occurs during your treatment with

BEDURAS, you must immediately inform your doctor and should use genetic consultation.

Men receiving treatment with bendamustine are advised not to father a child during treatment and for up to 6 months afterwards.

Before starting treatment, you should seek advice on storing sperm because of the possibility of permanent infertility.

Driving and using machines

BEDURAS may cause dizziness or lack of coordination. Take special care before driving a vehilce or operating machines that require your attention, until you know how you will react to BEDURAS.

3. How BEDURAS is given

BEDURAS is administered into a vein over 30 – 60 minutes in various dosages, either alone (monotherapy) or in combination with other medicines.

Treatment should not be started if your white blood cells (leukocytes) have fallen to counts below 3 x 10^9/L and/or your blood platelets have fallen to counts below 75 x 10^9/L.

Your doctor will determine these values at regular intervals.

Treatment should be terminated if white blood cell (leukocyte) and/or platelet values drop to ≤ 3 x 10^9/L or ≤ 75 x 10^9/L, respectively. Treatment can be continued after white blood cell values have increased to > 4 x 10^9/L and platelet values to > 100 x 10^9/L.

Impaired liver or kidney function

Dependent on the degree of impairment of your liver or kidney function it may be necessary to adjust your dose. Your attending doctor will decide whether a dosage adjustment is necessary.

How it is administered

Treatment with BEDURAS should be undertaken only by doctors experienced in cancer therapy.

Your doctor will give you the exact dose of BEDURAS and use the necessary precautions.

Your attending doctor will administer the solution for infusion after preparation as prescribed. The solution is administered into a vein as a short-term infusion over 30 – 60 minutes.

If you receive more BEDURAS than you should

Since a health care provider will administer BEDURAS, he/she will control the dosage. However, in the event of overdosage your doctor will manage the symptoms of the overdosage.

If you forget to receive BEDURAS

Since a health care provider will administer BEDURAS, it is unlikely that the dose will be missed.

4. Possible side effects

BEDURAS can have side effects.

Not all side effects reported for BEDURAS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving BEDURAS, please consult your doctor, pharmacist or other health care provider for advice.

If any of the following happens, stop receiving BEDURAS and tell your doctor immediately:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

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

Tissue death (necrosis) has been less frequently observed following unintentional injection into the tissue outside blood vessels (extravascular). A burning sensation where the infusion needle is inserted may be a sign of injection into tissue outside the blood vessels. This can cause pain and poorly healing skin defects.

BEDURAS can cause impaired bone marrow function, which usually returns to normal after treatment. Suppressed bone marrow function increases the risk of infection.

Tell your doctor if you notice any of the following:

Frequently occurring side effects:

- low counts of white blood cells (leukocytopenia)
- decrease in the red cells of the blood which can make the skin pale and cause weakness (anaemia)
- low counts of platelets (thrombocytopenia)
- low counts of neutrophils (neutropenia)
- hypersensitivity reactions such as allergic inflammation of the skin (dermatitis), nettle rash (urticaria)
- fatigue
- feeling sick (nausea)
- vomiting
- fever
- mucosal inflammation
- bleeding (haemorrhage)
- increased blood level of creatinine
- increased blood level of urea
- a rise in liver enzymes AST/ALT
- a rise in the enzyme alkaline phosphatase
- a rise in bile pigment
- low potassium blood levels
- impaired function (dysfunction) of the heart
- palpitations
- low or high blood pressure (hypotension or hypertension)
- impaired lung function

- disturbed metabolism caused by dying cancer cells releasing their contents into the bloodstream
- diarrhoea
- constipation
- dehydration
- sore mouth (stomatitis)
- hair loss
- skin changes
- missed periods (amenorrhoea)
- pain, chills
- insomnia.

Less frequently occurring side effects:

- accumulation of fluid in the heart sac (escape of fluid into the pericardial space)
- infection of the blood (sepsis)
- tuberculosis (TB)
- severe allergic hypersensitivity reactions (anaphylactic reactions)
- signs similar to anaphylactic reactions (anaphylactoid reactions)
- drowsiness
- loss of voice (aphonia)
- acute circulatory collapse
- reddening of the skin (erythema)
- inflammation of the skin (dermatitis)
- itching (pruritus)
- skin rash (macular exanthema)
- excessive sweating (hyperhidrosis)
- primary atypical inflammation of the lungs (pneumonia)

- break-down of red blood cells (haemolytic anaemia)
- rapid decrease in blood pressure sometimes with skin reactions or rash (anaphylactic shock)
- disturbed sense of taste
- altered sensations (paraesthesia)
- malaise and pain in the limbs (peripheral neuropathy)
- disease of the nervous system (anticholinergic syndrome)
- neurological disorders
- lack of coordination (ataxia)
- inflammation of the brain (encephalitis)
- increased heart rate (tachycardia)
- heart attack, chest pain (myocardial infarct)
- heart failure
- inflammation of the veins (phlebitis)
- formation of scar tissue in the lungs (fibrosis of the lungs)
- inflammation and bleeding of the gullet (haemorrhagic oesophagitis)
- bleeding of stomach or gut
- infertility
- multiple organ failure.

There have been reports of secondary tumours (myelodysplastic syndrome, acute myeloid leukaemia, bronchial carcinoma) following treatment with BEDURAS.
Severe skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis) have been reported.
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's website. By reporting side effects, you can help provide more information on the safety of BEDURAS.

5. How to store BEDURAS

Unopened vial:

- Store at or below 25 °C.
- Keep the vial in the outer carton in order to protect from light.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Solution for infusion:

- After reconstitution and dilution, chemical and physical stability has been demonstrated for 3,5 hours at 25 °C and 2 days at 2 °C to 8 °C in polyethylene bags.
- From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6. Contents of the pack and other information

What BEDURAS contains

The active substance is bendamustine hydrochloride.

BEDURAS 25 mg: 1 vial contains 25 mg of bendamustine hydrochloride (sterile active ingredient).

BEDURAS 100 mg: 1 vial contains 100 mg of bendamustine hydrochloride (sterile active ingredient).

The other ingredient is mannitol.

What BEDURAS looks like and contents of the pack

White to off white lyophilised powder or plug.

BEDURAS 25 mg: Type I amber glass vial of 20 mL with 20 mm grey bromobutyl double slotted lyo stopper and 20 mm aluminium flip-off red seals. Pack sizes: 1, 5, 10 or 20 vials.

BEDURAS 100 mg: Type I amber glass vial of 50 mL with 20 mm grey bromobutyl double slotted

lyo stopper and 20 mm aluminium flip-off red seals. Pack sizes: 1 or 5 vials.

Holder of Certificate of Registration

Pharma-Q Holdings (Pty) Ltd

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To follow

Registration numbers

BEDURAS 25 mg: 56/26/1123

BEDURAS 100 mg: 56/26/1124

Access to the corresponding Professional Information

https://www.pharmaq.co.za