PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

SPALBEND 25 or 100 (powder for concentrate for solution for infusion)

Bendamustine hydrochloride

SPALBEND 25: Contains sugar (mannitol 30 mg /vial)

SPALBEND 100: Contains sugar (mannitol 120 mg /vial)

Read all of this leaflet carefully before you are given **SPALBEND**

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

What is in this leaflet:

1. What SPALBEND is and what it is used for

SPALBEND is a medicine which is used for the treatment of certain types of cancer (cytotoxic medicine).

SPALBEND 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's lymphomas, which had not, or only shortly, responded to prior rituximab treatment
- Multiple myeloma in cases where high-dose chemotherapy with autologous stem cell transplantation, thalidomide or bortezomib containing therapy is not appropriate for you.

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

Do not take SPALBEND:

- if you are **allergic** to bendamustine hydrochloride or any of the other ingredients of **SPALBEND** (listed in section 6)
- if you are pregnant
- while **breastfeeding**, if treatment with **SPALBEND** is necessary during lactation you must discontinue breastfeeding (see section warnings and precautions on breastfeeding)
- if you have **severe liver dysfunction** (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 **severely disturbed bone marrow function** (bone marrow depression) and **serious changes** in your **number** of **white blood cells** and **platelets** in the blood
- 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 (**leukocytopenia**)
- In combination with **yellow fever vaccines.**

If you are not sure, talk to your doctor or pharmacist before you are given **SPALBEND.**

Warnings and precautions

Talk to your doctor or nurse before using **SPALBEND**:

- In case of **reduced capability of the bone marrow to replace blood cells.** Your doctor will have your number of white blood cells and platelets in the blood checked before starting treatment with **SPALBEND**, 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 **reactions on your skin** during treatment with **SPALBEND**. The 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 **SPALBEND**. 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.

Other medicines and SPALBEND

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

If **SPALBEND** is used in combination with medicines which inhibit the formation of blood in the bone marrow, the effect on the bone marrow may be intensified.

If **SPALBEND** is used in combination with medicines which alter your immune response, this effect may be intensified.

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).

Pregnancy, breast-feeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using **SPALBEND**.

Pregnancy

SPALBEND can cause genetic damage and has caused malformations in animal studies. You should not use **SPALBEND** if you are pregnant.

If you are a woman of childbearing potential you must use an effective method of contraception both before and during treatment with **SPALBEND**. If pregnancy occurs during your treatment with **SPALBEND** you must immediately inform your doctor and should have genetic consultation.

Breastfeeding

SPALBEND must not be administered during breastfeeding. If treatment with **SPALBEND** is necessary during lactation you must discontinue breastfeeding. Ask your doctor or pharmacist for advice before taking any medicine.

Fertility

Men receiving treatment with **SPALBEND** 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.

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Driving and using machines

SPALBEND has major influence on the ability to drive and to use machines have been performed. Do not drive or operate machines if you experience side effects, such as dizziness or lack of coordination.

3. How to use SPALBEND

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

Your doctor will prescribe the specific dosage regimen required for your condition.

Treatment will not be started if your white blood cells (leukocytes) and/or your blood platelets have fallen to counts below determined levels.

Your doctor will determine these values at regular intervals.

You will not be expected to give yourself **SPALBEND**. It will be given to you by a person who is qualified to do so.

Treatment may be terminated if white blood cell (leukocyte) and/or platelet values dropped to determined levels. Treatment can be continued after white blood cell and platelet values have increased.

Impaired liver or kidney function

Dependent on the degree of impairment of your liver function it may be necessary to adjust your dose (by 30 % in case of moderate liver dysfunction). No dose adjustment is necessary in case of impairment of kidney function. Your attending doctor will decide whether a dosage adjustment is necessary.

How it is administered

Treatment with **SPALBEND** should be undertaken only by doctors experienced in tumour therapy. Your doctor will give you the exact dose of **SPALBEND** 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.

Duration of use

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

If you are at all worried or have any questions regarding treatment with **SPALBEND**, please speak to your doctor or nurse.

If you forget to use SPALBEND

If a dose of **SPALBEND** has been forgotten, your doctor will usually retain the normal dosage schedule.

If you stop using SPALBEND

The doctor treating you will decide whether to interrupt the treatment or to change over to a different preparation.

4. Possible side effects

SPALBEND can have side effects.

Not all side effects reported for **SPALBEND** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **SPALBEND**, please consult your health care provider for advice.

Contact your doctor or seek medical attention immediately if you notice any of the following side effects:

• Difficulty breathing, swelling of the lips, itching or rash. This may be due to an allergic hypersensitivity) reaction.

• Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms

• widespread rash, high body temperature, enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome).

Tissue decay (necrosis) has been observed very rarely following leakage of bendamustine hydrochloride into the tissue outside the blood vessels (extravascular). A burning sensation where the infusion needle is inserted may be a sign of leakage outside the blood vessels. The consequence can be pain and poorly healing skin defects.

The dose-limiting side-effect of **SPALBEND** is impaired bone-marrow function, which usually returns to normal after treatment.

Suppressed bone marrow function may lead to low counts of blood cells, which in turn may lead to an increased risk of infection, anaemia or a heightened risk of bleeding.

Other side effects include:

Frequent:

• Low counts of white blood cells (disease-fighting cells in your blood)

• Decrease in the red pigment of the blood (haemoglobin: a protein in red blood cells that carries oxygen throughout the body)

• Low counts of platelets (colourless blood cells that help blood clot)

• Infections

• Feeling sick (nausea)

• Vomiting

• Mucosal inflammation

• Increased blood level of creatinine (a chemical waste product that is produced by your muscle)

• Increased blood level of urea (a chemical waste product)

• Fever

• Fatigue

• Headache

• Bleeding (haemorrhage)

• Disturbed metabolism caused by dying cancer cells releasing their contents into the blood stream

• Reduction in red blood cells which can make the skin pale and cause weakness or breathlessness (anaemia)

• Low counts of neutrophils (a common type of white blood cell important to fighting off infections)

• Abnormally low concentration of neutrophils (a type of white blood cell) in the blood leading to increased susceptibility to infection (neutropenia)

• Hypersensitivity reactions such as allergic inflammation of the skin (dermatitis), nettle rash (urticaria)

• 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)

• Disturbed function (dysfunction) of the heart

• Disturbed heart rhythms (arrhythmia)

• Low or high blood pressure (hypotension or hypertension)

• Disturbed lung function

• Diarrhoea

• Constipation

• Sore mouth (Stomatitis)

• Loss of appetite

• Hair loss

• Skin changes

• Missed periods (amenorrhoea)

• Pain

• Insomnia

• Chills

• Dehydration

• Dizziness

Less Frequent:

• Accumulation of fluid in the heart sac (escape of fluid into the pericardial space)

• Ineffective production of all blood cells in the bone marrow (the spongy material inside your bones where

blood cells are made)

• Acute leukemia

• Heart attack, chest pain (myocardial infarct)

• Heart failure

• Infection of the blood (sepsis)

• Severe allergic hypersensitivity reactions (anaphylactic reactions)

• Signs similar to anaphylactic reactions (anaphylactoid reactions)

• Drowsiness

• Loss of voice (aphonia)

• Acute circulatory collapse (failure of blood circulation mainly from a cardiac origin with failure to maintain the supply of oxygen and other nutrients to the tissues and removing toxins) Reddening of the skin (erythema)

• Inflammation of the skin (dermatitis)

• Itching (pruritus)

• Skin rash (macular exanthema)

• Excessive sweating (hyperhidrosis)

• Reduction in your bone marrow function, which may make you feel unwell or show up in your blood tests

• Primary atypical inflammation of the lungs (pneumonia)

• Break-down of red blood cells

• 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)

• Serious condition resulting in the blockade of specific receptor in the nervous systems

• Disorders of the nervous systemLack of coordination (ataxia)

• Inflammation of the brain (encephalitis)

• Increased heart rate (tachycardia)

• Inflammation of the veins (phlebitis)

• Formation of tissue in the lungs (fibrosis of the lungs)

• Bleeding inflammation of the gullet (haemorrhagic oesophagitis)

• Bleeding of stomach or gut

• Infertility

• Multiple organ failure

Frequency unknown:

• Renal failure

• Liver failure

• Irregular and often rapid heart rate (atrial fibrillation)

• Painful red or purplish rash that spreads and blisters and/or other lesions begin to appear in the mucous membranes

(e.g. mouth and lips), in particular if you had before light sensitivity, infections of the respiratory system (e.g. bronchitis) and/or fever.

• Pneumonitis

• Bleeding from the lungs

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

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **SPALBEND.**

5. How to store SPALBEND

Store at or below 25 °C.

Keep the vial in the outer carton in order to protect from light.

Keep out of reach of children

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Ask your pharmacist how to dispose of medicines you no longer use.

6. Contents of the pack and other information

What SPALBEND contains

The active substance is bendamustine hydrochloride.

The other ingredients are: mannitol

What SPALBEND looks like and contents of the pack

SPALBEND 25: Type I amber glass vials of 20 ml with 20 mm bromobutyl (single slotted) lyo stopper along with 20 mm easy to open C/L ALU, seals with matte finish plastic german blue in packs of 1, 5 or 10

SPALBEND 100: Type I amber glass vials of 50 ml with 20 mm bromobutyl (single slotted) lyo stopper along with 20 mm easy to open C/L ALU, seals with matte finish plastic german blue in in packs of 1, 5 or 10

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Ruby Pharmaceuticals (PTY) LTD

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