1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

SPALBORT 3,5 mg powder for solution for injection

Bortezomib

Contains sugar: 35 mg mannitol per vial

Read all of this leaflet carefully before you are given SPALBORT 3,5 mg

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

What is in this leaflet:

1. What SPALBORT 3,5 mg is and what it is used for

SPALBORT 3,5 mg belongs to a group of medicines called cytotoxic medicinal products. These are used to kill cancer cells.

SPALBORT 3,5 mg is used for the treatment of Multiple Myeloma (a cancer of the bone marrow) in adults:

• In combination with other medicines (melphalan and prednisone), for patients who have not been previously treated for Multiple Myeloma.

• Alone (monotherapy) for patients whose disease is worsening (progressive) after receiving at least one prior treatment for Multiple Myeloma.

• Mantle Cell Lymphoma (a blood cancer in the lymph glands) in adults whose disease is worsening (progressive) after receiving at least one prior treatment, one of which should have included the medicine anthracycline (or mitoxantrone) and/or rituximab as part of their chemotherapy treatment.

2. What you need to know before you receive SPALBORT 3,5 mg

You must not receive SPALBORT 3,5 mg:

- If you are allergic (hypersensitive) to bortezomib (active substance) or to any of the other ingredients of SPALBORT 3,5 mg (listed in section 6)
- if you have severe liver problems.
- if you have certain severe lung or heart problems.

Warnings and precautions

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

Special care should be taken with SPALBORT 3,5 mg:

• If you have a low level of red blood cells, platelets, or white blood cells, as these conditions may become worse during treatment with SPALBORT 3,5 mg.

• If you have had any bleeding problems.

• If you are suffering from diarrhoea, constipation or nausea and vomiting, as this may become worse during SPALBORT 3,5 mg treatment.

• If you have a history of fainting, dizziness or lightheadedness.

• If you have any problems with your kidneys.

• If you have any problems with your liver or previous liver infection known as hepatitis B.

• If you have had any problems in the past with numbness, tingling, or pain in the hands or feet (peripheral neuropathy). This effect may become worse during SPALBORT 3,5 mg treatment.

• If you have any problems with your heart or with your blood pressure or swelling of your body (fluid retention) and especially if you take medicines for these conditions.

• lung problems with symptoms such as shortness of breath or cough.

• seizures (fits)

• Herpes zoster, also known as shingles (localised painful skin rash spread across the body or around the eyes)

• If you have been diagnosed with a condition called amyloidosis (that results from the abnormal deposit of particular protein (called amyloid), in various tissues of the body).

• symptoms of a so-called ‘tumor lysis syndrome’, such as muscle cramping, muscle weakness, confusion, visual loss or disturbances and shortness of breath.

• headaches, seizures (fits), confusion, changed mental state, vision loss and high blood pressure. These might be symptoms of a neurological disorder called ‘posterior reversible encephalopathy syndrome’.

• memory loss, trouble thinking, difficulty with walking or loss of vision. These may be signs of a very rare but serious brain infection known as ‘progressive multifocal leukoencephalopathy’ (PML) and your doctor may suggest further testing and follow-up.

You will have to take regular blood tests before and during your treatment with SPALBORT 3,5 mg, to check your blood cell counts regularly.

If you have mantle cell lymphoma and are given SPALBORT 3,5 mg you should tell your doctor.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine.

Children and adolescents

SPALBORT 3,5 mg has not been studied in children or adolescents and therefore should not be used in this patient population.

Other medicines and SPALBORT 3,5 mg

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines.) The use of SPALBORT 3,5 mg with these medicines may cause undesirable interactions.

In particular tell your doctor if you are using medicines containing the following active substances:

- Ketoconazole and other azole antifungals used to treat fungal infections.
- rifampicin, an antibiotic used to treat bacterial infections.
- carbamazepine, phenytoin or phenobarbital used to treat epilepsy.
- St. John's Wort used for depression or other conditions.
- Oral antidiabetic medication.

Pregnancy, breast-feeding 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 receiving this medicine.

SPALBORT 3,5 mg must not be used if you are pregnant or breastfeeding.

You must make sure that you do not become pregnant while receiving SPALBORT 3,5 mg. Both men and women must ensure adequate birth control measures are taken whilst receiving SPALBORT 3,5 mg, and for 3 months after treatment.

If you do become pregnant or are breastfeeding your baby while receiving SPALBORT 3,5 mg, please consult your doctor, pharmacist or other health care professional for advice.

If you wish to restart breastfeeding after SPALBORT 3,5 mg treatment, you must discuss this with your doctor, pharmacist or other health care professional, who will tell you when it is safe to do so.

Driving and using machines

SPALBORT 3,5 mg might cause low blood pressure that may lead to tiredness, dizziness, fainting, or blurred vision. Do not drive or operate tools or machines if you experience such side effects. Even if you have not felt these effects, you must still be cautious.

3. How SPALBORT 3,5 mg powder for injection is given

You will be given SPALBORT 3,5 mg intravenously or subcutaneously (under the skin).

SPALBORT 3,5 mg is for intravenous or subcutaneous use.

You will receive SPALBORT 3,5 mg in a specialised medical unit, under the supervision of a doctor experienced in the use of cytotoxic medicinal products.

SPALBORT 3,5 mg powder has to be dissolved before administration. This will be done by a healthcare professional. The resulting solution is then either injected into a vein or under the skin.

Injection into the vein is rapid, taking 3 to 5 seconds.

Injection under the skin is in either the thigh or the abdomen.

The dose will be calculated from your height and weight (body surface area).

Monotherapy

When SPALBORT 3,5 mg is given alone, one cycle of treatment with SPALBORT 3,5 mg consists of a total of 4 doses. Doses are given on days 1, 4, 8 and 11, followed by a 10-day ‘rest period’ without treatment.

Therefore, the duration of a treatment cycle is 21 days (3 weeks).

Combination therapy

If you have not been treated before for multiple myeloma, you will receive SPALBORT 3,5 mg together with two other medicines containing melphalan and prednisone.

In this case, the duration of a cycle is 6 weeks. The treatment consists of a total of 9 cycles (54 weeks).

• In cycles 1 to 4, SPALBORT 3,5 mg is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.

• In cycles 5 to 9, SPALBORT 3,5 mg is administered once weekly on days 1, 8, 22 and 29.

Melphalan and prednisone are both given orally on days 1, 2, 3 and 4 of the first week of each cycle.

If you receive more SPALBORT 3,5 mg than you should:

Since a healthcare professional will administer SPALBORT 3,5 mg**,** he/she will control the dosage.

In the event of overdosage, the doctor will treat you.

If you miss a dose of SPALBORT 3,5 mg:

SPALBORT 3,5 mg will be administered under your doctor's supervision.

If you think you have not been given a dose of SPALBORT 3,5 mg, tell your doctor or other healthcare professional immediately.

4. Possible side effects

SPALBORT 3,5 mg can cause side-effects.

Not all side effects reported for SPALBORT 3,5 mg are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving SPALBORT 3,5 mg, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following happens, stop receiving SPALBORT 3,5 mg and tell your doctor immediately or go to the casualty department at your nearest hospital:

• swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing

• rash or itching

• fainting

• yellowing of the skin and eyes, also called jaundice.

These are all very serious side effects. If you have them, you may have had a serious reaction to SPALBORT 3,5 mg. 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:

• muscle cramping, muscle weakness

• coughing and breathing difficulties or tightness in the chest.

• confusion, visual loss or disturbances, blindness, seizures (fits), headaches

• shortness of breath, swelling of your feet or changes in your heart beat, high blood pressure, tiredness

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

Tell your doctor if you notice any of the following which may occur frequently:

• herpes zoster, also known as shingles (localised painful skin rash spread across the body or around the eyes), herpes simplex virus infection (skin blisters or cold sores), fungal infections

• decrease in the number of red blood cells, which can cause anaemia with symptoms such as tiredness and paleness

• decrease in the number of white blood cells which may make you more prone to infections or flu like symptoms

• decrease in the number of platelets in your blood which may make you more prone to bruising, or to bleeding without obvious injury

• decreased appetite, dehydrated (feeling thirsty)

• mood swings, anxiety, sleep disturbances

• sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet due to nerve damage, dizziness, taste disturbances, feeling drowsy and indifferent (lethargy), loss of consciousness

• eye swelling, abnormal vision, infection of the outermost layer of the eye and the inner surface of the eyelids (conjunctivitis)

• low blood pressure, sudden fall of blood pressure on standing which may lead to fainting

• nose bleeds, chest infection

• feeling sick (nausea) or vomiting, diarrhoea (loose stools), constipation, heartburn, mouth sores, bloating, belching, wind, stomach pain, bleeding from your bowels or stomach

• itching of the skin, red lumps on the skin or dry skin

• abnormal blood sugar levels.

• reduced functioning of your kidneys (decreased urination)

• fever, tiredness (fatigue), feeling weak, swelling of body, general ill feeling, shivering, pain

• muscle pain, pain in arm or legs

• weight loss

Tell your doctor if you notice any of the following which may occur less frequently:

• infections, including chest, skin, ear and tooth infections

• benign or malignant tumours, cancer of the kidney

• blood clot in small blood vessels (thrombotic microangiopathy)

• thyroid gland disorders

• vitamin B deficiency, gout (painful swelling of joints), increased appetite, inability to tolerate alcohol consumption.

• hallucinations (seeing or hearing things), confusion, suicidal thoughts, stress-related mental illness (adjustment disorder), disorientation, decreased sex drive

• trembling, twitching, abnormal movements, balance disturbances, memory loss, speech disorder, restless leg syndrome, migraine, disturbance in attention, stroke (bleeding in the brain), coma, drooling, paralysis

• serious nerve inflammation, which may cause paralysis and difficulty breathing (Guillain-Barré syndrome)

• bleeding in eye, eye pain, dry eye, eye irritation, decreased tears, eye discharge, light sensitivity. eye irritation, eyelid infection, visual impairment upto blindness.

• lump in the eyelid (chalazion) and red and swollen eyelids

• hearing loss, deafness or ringing in the ears, ear discomfort, ear disorder which may cause dizziness, balance problems

• heart failure, heart attack, chest pain, chest discomfort, increased or reduced heart rate, inflammation of the lining around your heart or fluid around your heart

• inflammation of a vein, flushes, blood clots in your veins and lungs, problems with blood clotting, insufficient circulation

• disorders that affect your lungs, preventing your body from getting enough oxygen some of these include difficulty breathing, shortness of breath, difficulty breathing (becomes shallow or stops), wheezing, difficulty breathing during sleep, coughing blood, throat tightness, dry throat, throat irritation, runny nose

• infections or inflammation of the mouth, oesophagus, stomach and intestines, sometimes associated with pain or bleeding, mouth ulcers, poor movement of the intestines (including blockage), bleeding gums, coated tongue, abdominal or throat discomfort, difficulty swallowing, vomiting of blood

• swelling of the liver, bleeding from the liver

• inflammation or haemorrhage of the blood vessels that can appear as small red or purple dots (usually on the legs) to large bruise like patches under the skin or tissue, increased sweating, acne, nail disorder

• arthritis, including inflammation of the joints in the fingers, toes, and the jaw, lower back pain and leg pain, unpleasant sensations in the legs

• increased or decreased urine production (due to kidney damage), painful passing of urine or blood/proteins in the urine, fluid retention, bladder infection

• vaginal bleeding, genital pain, difficulty with erections, pain in the pelvis area, breast disorders, vaginal tears

• bruises, falls and injuries

• angioedma (swelling underneath the skin), Amyloidosis (a rare disease that occurs when a protein called amyloid builds up in organs), Type III-immune complex mediated reactions (abnormal immune response is mediated by the formation of antigen-antibody aggregates called "immune complexes)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 SPALBORT 3,5 MG

5. How to store SPALBORT 3,5 mg

Store all medicines out of reach of children.

Store at or below 30 °C

Store in the original package to protect from light

Contents of the pack and other information

What SPALBORT 3,5 mg contains

- The active substance is bortezomib
- The other ingredients are:
- Mannitol, pyrogen free, water for injection

What SPALBORT 3,5 mg looks like and contents of the pack

SPALBORT 3,5 mg is a white to off white lyophilised powder or cake, filled in clear single use 10 ml Type I glass vial sealed with 20 mm grey bromobutyl rubber stopper and Aluminium flip-off seal of purple colour button. 1 vial in unit carton

Holder of Certificate of Registration

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