PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

BORTURAS 3,5 mg powder for solution for injection

Bortezomib

Contains mannitol (35 mg per vial).

Read all of this leaflet carefully before you start receiving BORTURAS

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

What is in this leaflet

1. What BORTURAS is and what it is used for

BORTURAS belongs to a group of medicines called cytotoxic medicines. These medicines are used to kill cancer cells.

BORTURAS is used for the treatment of multiple myeloma (a cancer of the bone marrow) and mantle cell lymphoma (a blood cancer in the lymph glands) in adults. It may be used alone or in combination with medicines.

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

BORTURAS should not be administered to you:

- If you are hypersensitive (allergic) to bortezomib or to any of the other ingredients of BORTURAS listed in section 6 of this leaflet.
- If you suffer from diseases of the heart or lungs.

Warnings and precautions

Special care should be taken with BORTURAS:

- If you are suffering from diarrhoea, constipation, nausea (feeling sick) or vomiting (being sick).
- If you have unexplained bleeding or bruising. Your doctor will conduct tests to monitor blood counts.
- If you experience a painful, usually itchy, rash that develops on one side of the face or body, you may have shingles.
- If you experience clumsiness, weakness, or difficulty speaking or thinking – you may be experiencing a side effect of BORTURAS.
- If you have experienced numbness, tingling, or pain in your hands or feet (neuropathy) in the past.
- If you suffer from seizures.
- If you experienced fainting, dizziness or light-headedness in the past.
- If you heart or blood pressure problems.
- If you have experienced or have new or increased shortness of breath or cough.
- If you have any problems with your kidneys.
- If you have any problems with your liver.
- If you experience symptoms of tumour lysis syndrome, such as muscle cramping, muscle weakness, confusion, visual loss or disturbances and shortness of breath.
- If you have been diagnosed with a condition called amyloidosis (that results from the abnormal deposit of a particular protein (called amyloid), in various tissues of the body).

If you have mantle cell lymphoma and are given the medicine rituximab with BORTURAS, you should

tell your doctor:

- if you think you have hepatitis infection now or have had it in the past. In a few cases, patients who have had hepatitis B might have a repeated attack of hepatitis, which can be fatal. If you have a history of hepatitis B infection you will be carefully checked by your doctor for signs of active hepatitis B.

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

You must read the package leaflets of all medicines to be taken in combination with BORTURAS for information related to these medicines before starting treatment with BORTURAS.

Children and adolescents

BORTURAS should not be used in children and adolescents because it is not known how the medicine will affect them.

Other medicines and BORTURAS

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

Tell your doctor or pharmacist before you receive BORTURAS if you are taking other medicines, in particular medicines containing the following active substances:

- ketoconazole (used to treat fungal infections) or ritonavir (used to treat human immunodeficiency virus (HIV) infection), as it may increase the blood concentration of BORTURAS resulting in a higher risk for side effects and toxicity,
- rifampicin (an antibiotic used to treat bacterial infections), as it may reduce the blood concentration of BORTURAS and efficacy may be reduced,
- carbamazepine, phenytoin or phenobarbital (used to treat epilepsy), as it may reduce the blood

concentration of BORTURAS and efficacy may be reduced,

- St. John's Wort (*Hypericum perforatum*) (used for depression or other conditions), as it may reduce the blood concentration of BORTURAS and efficacy may be reduced,
- narcotics, also known as opioids (used to treat severe pain), as it may increase the risk of constipation, nausea and vomiting,
- oral antidiabetic medicines, as it may result in higher or lower blood sugar levels. If you are taking oral antidiabetic medicines and is receiving BORTURAS, your doctor should closely monitor your blood glucose levels and may need to adjust your dose of antidiabetic medicines.
- medicines associated with peripheral neuropathy (weakness, numbness and pain from nerve damage, usually in the hands and feet), such as amiodarone (used to treat irregular heartbeat), anti-viral medicines, isoniazid (used to treat tuberculosis), nitrofurantoin (antibiotic medicine used to treat lower urinary tract infections) or statins (used to lower your cholesterol levels) as the risk for peripheral neuropathy may be increased.

Pregnancy and breastfeeding

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 BORTURAS.

Avoid pregnancy while being treated with BORTURAS. Both men and women should use adequate contraception during treatment, and for at least 3 months after receiving the last dose. If you become pregnant while on treatment with BORTURAS, immediately inform your doctor who will decide if treatment should be continued. Do not breastfeed your baby while being treated with BORTURAS.

Driving and using machines

BORTURAS might cause tiredness, dizziness, fainting, or blurred vision. Do not drive a vehicle or operate machines if you experience such side effects; even if you do not, you should still be cautious. It is not always possible to predict to what extent BORTURAS may interfere with your daily activities.

Do not engage in the above activities until you are aware of the measure to which BORTURAS affects you.

3. How BORTURAS will be administered to you

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

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

You will receive BORTURAS in a specialised medical unit, under the supervision of a doctor experienced in the use of cytotoxic medicines.

BORTURAS is for intravenous or subcutaneous use.

BORTURAS powder has to be dissolved before administration. This will be done by a health care professional. The resulting solution is then injected under the skin or into a vein.

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

Your doctor will calculate your dose of BORTURAS according to your height and weight (body surface area).

Your doctor will also tell you how many treatment cycles you will have. You will have dosing days and rest days (where no treatment is given).

Your doctor may change the dose and total number of treatment cycles, depending on your response to the treatment on the occurrence of certain side effects.

Your doctor will tell you how long your treatment with BORTURAS will last. Do not stop treatment early unless your doctor tells you to do so.

If you have the impression that the effect of BORTURAS is too strong or too weak, tell your doctor or pharmacist.

If you receive more BORTURAS than you should

Since a health care provider will administer BORTURAS, he / she will control the dosage. However, in

the event of overdosage your doctor will manage the overdosage.

If you forget to use BORTURAS

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

If you stop using BORTURAS

It is important to keep receiving BORTURAS, as long as your doctor prescribes it for you. If you have any further questions on the use of BORTURAS, ask your doctor or pharmacist.

4. Possible side effects

BORTURAS can have side effects.

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

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

- swelling of your 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 BORTURAS. You may need urgent medical attention or hospitalisation.

Treatment with BORTURAS can frequently cause a decrease in the numbers of red and white blood cells and platelets in your blood. Therefore, you will have to take regular blood tests before and during your treatment with BORTURAS, to check your blood cell counts regularly. You may experience a reduction in the number of:

- platelets, which may make you be more prone to bruising or to bleeding without obvious injury (e.g. bleeding from your bowels, stomach, mouth and gum or bleeding in the brain or bleeding from the liver),
- red blood cells, which can cause anaemia, with symptoms such as tiredness and paleness,
- white blood cells may make you more prone to infections or flu-like symptoms.

Frequent side effects:

- sensitivity, numbness, tingling or burning sensation of the skin or pain in the hands or feet, due to nerve damage,
- fever,
- feeling sick (nausea) or vomiting (being sick), loss of appetite,
- constipation with or without bloating (can be severe),
- diarrhoea: if this happens, it is important that you drink more water than usual. Your doctor may give you another medicine to control diarrhoea,
- tiredness (fatigue), feeling weak,
- low blood pressure, sudden fall of blood pressure on standing which may lead to fainting,
- high blood pressure,
- reduced functioning of your kidneys (swelling of your feet and ankles, nausea, vomiting, weakness),
- headache,
- general ill feeling, pain, vertigo, light-headedness, a feeling of weakness or loss of consciousness,
- shivering,
- infections, including pneumonia, respiratory infections, bronchitis, fungal infections, coughing with phlegm, flu like illness,
- shingles (localised including around the eyes or spread across the body),
- changes in potassium, sodium or calcium in your blood, too much sugar in your blood when blood tests are done (warning signs may include muscle weakness, muscle cramps, numbness, chest pain, shortness of breath, irregular heartbeat, pounding of your heart, feeling tired, extreme thirst,

nausea, headache, confusion, sensation of pins-and-needles, frequent urination and blurred vision),

- chest pains or shortness of breath with exercise,
- different types of rash,
- itching of the skin, lumps on the skin or dry skin,
- facial blushing or tiny broken capillaries,
- redness of the skin,
- Dehydration (increased thirst, dry mouth, swollen tongue, weakness, confusion),
- heartburn, bloating, belching, wind, stomach pain, bleeding from your bowels or stomach (you may notice blood in your stool or vomit),
- alteration of liver functioning, including jaundice and hepatitis (yellowing of your skin and eyes, dark urine, stomach pain, feeling tired, fever),
- a sore mouth or lip, dry mouth, mouth ulcers or throat pain,
- weight loss, loss of taste,
- muscle cramps, muscle spasms, muscle weakness, pain in your limbs,
- blurred vision,
- infection of the outermost layer of the eye and the inner surface of the eyelids (conjunctivitis),
- nose bleeds,
- difficulty or problems in sleeping, anxiety, mood swings,
- swelling of body, including around eyes and other parts of the body.

Less frequent side effects:

- palpitations (sensation of rapid or irregular heart beat), chest pain, chest discomfort, which may indicate a heart problem,
- failing of your kidneys (passing less urine than is normal for you, swelling of your legs, ankles or feet, loss of appetite, nausea, vomiting, extreme tiredness, shortness of breath, muscle cramps),
- throbbing pain or swelling in one leg, redness, or pale fingers and toes may indicate a problem with your circulation or formation of blood clots,

- sweating, restlessness, changes in your mental status, seeing or hearing things that don't exist, disorientation, irritability, depression,
- infections including urinary tract infections, the flu, herpes virus infections, ear infection and cellulitis – you may experience fever, chills, sweating, pain,
- bloody stools or bleeding from mucosal membranes, e.g. mouth, vagina,
- cerebrovascular disorders, stroke (sudden weakness or numbness on one side of your body, severe headache, vision problems, slurred speech, dizziness, confusion),
- paralysis, seizures, falling, movement disorders, abnormal or change in, or reduced sensation (feeling, hearing, tasting, smelling), attention disturbance, trembling, twitching,
- serious nerve inflammation, which may cause paralysis and difficulty breathing (Guillain-Barré syndrome),
- changes in magnesium and phosphates in your blood when blood tests are done (warning signs may include muscle weakness, muscle cramps, tremors, twitches, irritability, insomnia, numbness and tingling, severe drowsiness, fatigue, confusion, fast or irregular heartbeat, thirst, sensation of pins-and-needles),
- arthritis, including inflammation of the joints in the fingers, toes and the jaw,
- disorders that affect your lungs, preventing your body from getting enough oxygen. Some of these include difficulty breathing, shortness of breath, shortness of breath without exercise, breathing that becomes shallow, difficult or stops, wheezing,
- hiccups, speech disorders,
- increased or decreased urine production (due to kidney damage), painful passing of urine or blood/proteins in the urine, fluid retention,
- altered levels of consciousness, confusion, memory impairment or loss,
- hearing loss, deafness or ringing in the ears, ear discomfort,
- hormone abnormality which may affect salt and water absorption (dry mouth, thirst, confusion, muscle weakness or spasms, heart palpitations, slow or irregular heartbeat, itching, extreme tiredness),
- inability to produce enough insulin or resistance to normal levels of insulin (feeling thirsty, needing

to urinate more often than usual, blurred vision, feeling tired, losing weight unintentionally),

- irritated or inflamed eyes, excessively wet eyes, painful eyes, dry eyes, eye infections, lump in the eyelid (chalazion), red and swollen eyelids, discharge from the eyes, abnormal vision, bleeding of the eye,
- swelling of your lymph glands,
- joint or muscle stiffness, sense of heaviness, pain in your groin,
- hair loss and abnormal hair texture,
- redness or pain at the injection site,
- mouth ulcers, pain or bleeding, stomach pain, difficulty swallowing, coughing or vomiting of blood,
- inflammation of the pancreas (pain in the upper stomach area that radiates to your back, tenderness, nausea, vomiting, fever), obstruction of the bile duct (light-colured stools, dark urine, pain in the upper right side of your stomach, nausea, vomiting),
- genital pain, problem having an erection,
- weight increase,
- thirst,
- severe forms of skin reactions (which may be life threatening), sometimes accompanied by fever, causing a painful, red, blistering or peeling skin rash. These may be signs of a condition known as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN), skin ulcers,
- skin rash or skin lesions with a pink/red ring and a pale centre which may be itchy, painful, scaly or filled with fluid. The rash may appear especially on the palms or soles of your feet. These could be signs of a serious skin condition called “erythema multiforme”.
- bruises, falls and injuries,
- 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,
- benign cysts of the spine (synovial cysts), which are fluid-filled sacs that develop along your spine with symptoms such as pain, tingling or cramping in the lower back and legs and difficulty walking,
- posterior reversible encephalopathy syndrome (PRES), a severe reversible brain condition which includes seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision

problems,

- flushing,
- discolouration of the veins,
- inflammation of the spinal nerve (sharp pain in your back, arms, legs or shoulders that may worsen with certain activities, even something as simple as coughing or sneezing, weakness or loss of reflexes in your arms or legs),
- problems with your ear, bleeding from your ear,
- underactivity (tiredness, dry skin or weight gain) or overactivity (rapid or irregular heartbeat, sweating, irritability, weight loss) of your thyroid gland,
- Budd–Chiari syndrome (disorder characterised by blockage of the liver veins) with symptoms such as pain in the upper right part of the stomach, extreme tiredness, nausea and jaundice (yellowing of your skin and white part of your eyes, dark urine),
- changes in or abnormal bowel function,
- bleeding in the brain (sudden or severe headache, weakness or numbness in one side of your body, nausea or vomiting, dizziness, confusion, difficulty speaking),
- breast disorders, vaginal tears, genital swelling,
- inability to tolerate alcohol consumption,
- wasting, or loss of body mass,
- increased appetite,
- fistula (opening on the skin around the anus with a red inflamed area around the tunnel opening and oozing of pus, blood or stool from the tunnel opening, pain in the rectum and anus, fever),
- pain, redness or stiffness in your joints,
- fracture,
- breakdown of muscle fibers which may cause dark, reddish urine, a decreased amount of urine, weakness and muscle aches,
- psoriasis like skin condition, paleness of the skin,
- partial or total loss of vision,
- decreased sex drive,

- drooling,
- sensitivity to light,
- rapid breathing,
- hernia,
- brittle or weak nails,
- coma,
- intestinal ulcers.

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 or pharmacist. This includes any possible side effects not listed in this leaflet. 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 BORTURAS.

5. How BORTURAS should be stored

- Store at or below 25 °C.
- Keep the vail in the outer carton in order to protect from light.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton or vial.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What BORTURAS contains

The active substance in BORTURAS is bortezomib.

For SC use: After reconstitution, 1 mL of solution for subcutaneous injection contains 2,5 mg

bortezomib.

For IV use: After reconstitution, 1 mL of solution for intravenous injection contains 1 mg bortezomib.

The other ingredient is:

Mannitol (E421).

What BORTURAS looks like and contents of the pack

A white to off white colour, lyophilised powder or plug

BORTURAS is packed in 10 mL, 20 mm flint flat bottom tubular USP type-I glass vials with 20 mm dark grey bromobutyl rubber stoppers (RFS) and 20 mm aluminium seal with light blue colour flip-off cap.

One vial is packed in an outer carton.

Holder of certificate of registration

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To follow

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Access to the corresponding Professional Information

https://www.pharmaq.co.za