PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

BORTEZOMIB ZYDUS 3,5 mg powder for solution for injection

Bortezomib

Contains mannitol.

Read all of this leaflet carefully before you start receiving BORTEZOMIB ZYDUS.

- 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 BORTEZOMIB ZYDUS is and what it is used for

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

BORTEZOMIB ZYDUS 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 use BORTEZOMIB ZYDUS

BORTEZOMIB ZYDUS should not be administered to you

- If you are hypersensitive (allergic) to bortezomib or to any of the other ingredients of BORTEZOMIB ZYDUS listed in section 6 of this leaflet.
- If you have certain severe lung or heart problems.

Warnings and precautions

Special care should be taken with BORTEZOMIB ZYDUS:

- If you are suffering from diarrhoea, constipation, nausea or vomiting.
- If you have bleeding problems and/or a low number of platelets in your blood.
- If you have a low level of red blood cells or white blood cells, as these conditions may become worse during treatment with BORTEZOMIB ZYDUS.
- 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 have 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 disorder where your body makes abnormal proteins (amyloidosis).
- If you experience symptoms of a very rare brain infection, namely progressive multifocal leukoencephalopathy (PML), such as memory loss, vision problems, clumsiness, weakness of your legs and arms and personality changes.

If you have mantle cell lymphoma and are given the medicine rituximab with BORTEZOMIB ZYDUS 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 BORTEZOMIB ZYDUS, to check your blood cell counts regularly.

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

Children and adolescents

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

Other medicines and BORTEZOMIB ZYDUS

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 BORTEZOMIB ZYDUS if you are taking other medicines, in particular medicines containing the following active substances:

- ketoconazole (used to treat fungal infections)
- ritonavir (used to treat human immunodeficiency virus [HIV] infection)
- rifampicin (an antibiotic used to treat bacterial infections)
- carbamazepine, phenytoin or phenobarbital (used to treat epilepsy)
- St John's wort (*Hypericum perforatum*) (used for depression or other conditions)
- oral antidiabetics.

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 BORTEZOMIB ZYDUS.

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

Driving and using machines

BORTEZOMIB ZYDUS might cause tiredness, dizziness, fainting or blurred vision. Do not drive a vehicle or operate tools or machines if you experience such side effects; even if you do not, you should still be cautious.

3. How to use BORTEZOMIB ZYDUS

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

You will not be expected to give yourself BORTEZOMIB ZYDUS. It will be given to you by a person

who is qualified to do so.

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

BORTEZOMIB ZYDUS is for intravenous or subcutaneous use.

BORTEZOMIB ZYDUS powder has to be dissolved before administration. This will be done by a health care provider. 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 work out your dose of BORTEZOMIB ZYDUS according to your height and weight (body surface area).

The usual starting dose of BORTEZOMIB ZYDUS is 1,3 mg/m^2 body surface area twice a week.

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

Your doctor will tell you how long your treatment with BORTEZOMIB ZYDUS will last. Do not stop treatment early.

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

If you take more BORTEZOMIB ZYDUS than you should

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

If you forget to use BORTEZOMIB ZYDUS

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

If you stop using BORTEZOMIB ZYDUS

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

4. Possible side effects

BORTEZOMIB ZYDUS can have side effects.

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

If any of the following happens, stop using BORTEZOMIB ZYDUS and tell your doctor 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 BORTEZOMIB ZYDUS. You may need urgent medical attention or hospitalisation.

If you are given BORTEZOMIB ZYDUS for multiple myeloma or mantle cell lymphoma, tell your doctor immediately if you notice any of the following symptoms: muscle cramping, muscle weakness, confusion, visual loss or disturbances, blindness, seizures, headaches, shortness of breath, swelling of your feet or changes in your heartbeat, high blood pressure, tiredness, fainting, coughing and breathing difficulties or tightness in the chest.

Treatment with BORTEZOMIB ZYDUS can 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 BORTEZOMIB ZYDUS, 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, which may make you more prone to infections or flu-like symptoms.

Tell your doctor if you notice any of the following:

Frequently occurring side effects

- sensitivity, numbness, tingling or burning sensation of the skin or pain in the hands or feet, due to nerve damage
- reduction in the number of red blood cells and/or white blood cells (see above)
- fever
- nausea (feeling sick) 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
- muscle pain, bone pain
- low blood pressure, sudden fall of blood pressure on standing which may lead to fainting
- high blood pressure
- reduced functioning of your kidneys
- headache
- tremor
- general ill feeling, pain, vertigo, light-headedness, a feeling of weakness or loss of consciousness
- 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)
- chest pains or shortness of breath with exercise
- different types of rash, eczema
- itching of the skin, lumps on the skin or dry skin
- facial blushing or tiny broken capillaries
- redness of the skin
- dehydration
- heartburn, bloating, belching, wind, stomach pain, bleeding from your bowels or stomach
- change in liver functioning
- a sore mouth or lips, dry mouth, mouth ulcers or throat pain
- weight loss, loss of taste
- muscle cramps, muscle spasms, muscle weakness, pain in your limbs, back pain, bone pain
- 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, sweating, anxiety, mood swings, depressed mood, changes in your mental status, disorientation
- swelling of your body, including around the eyes and other parts of the body
- mouth ulcers.

Less frequently occurring side effects

- heart failure, heart attack, chest pain, chest discomfort, increased or reduced heart rate
- failing of your kidneys
- inflammation of a vein, blood clots in your veins and lungs, problems with blood clotting, insufficient circulation, inflammation of the lining around your heart or fluid around your heart
- infections, including urinary tract infections, the flu, herpes virus infections, ear infection and cellulitis

- bloody stools or bleeding from mucosal membranes, e.g. mouth, vagina
- cerebrovascular disorders
- paralysis, seizures, falling, movement disorders, abnormal or change in, or reduced sensation (feeling, hearing, tasting, smelling), attention disturbance, twitching
- 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
- overactive thyroid gland
- inability to produce enough insulin or resistance to normal levels of insulin
- 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, buttock pain
- hair loss and abnormal hair texture
- redness or pain at the injection site
- mouth pain
- infections or inflammation of the mouth, oesophagus, stomach and intestines, sometimes associated with pain or bleeding, poor movement of the intestines (including blockage), abdominal or oesophageal discomfort, difficulty swallowing, vomiting of blood
- skin infections, bacterial and viral infections, tooth infection, fungal infections

- inflammation of the pancreas, obstruction of the bile duct
- genital pain, problem having an erection
- weight increase
- thirst
- hepatitis
- injection site or injection device-related disorders
- skin reactions and disorders (which may be severe and life threatening), skin ulcers
- 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
- a severe reversible brain condition which includes seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems
- heart problems, including heart attack, angina
- flushing
- discolouration of the veins
- inflammation of the spinal nerve
- problems with your ear, bleeding from your ear
- underactivity of your thyroid gland
- Budd–Chiari syndrome (the clinical symptoms caused by blockage of the hepatic veins)
- changes in or abnormal bowel function
- bleeding in the brain
- yellow discolouration of eyes and skin (jaundice)
- breast disorders, vaginal tears, genital swelling
- inability to tolerate alcohol consumption
- wasting, or loss of body mass
- increased appetite
- fistula

- joint effusion
- cysts in the lining of joints (synovial cysts)
- fracture
- breakdown of muscle fibres leading to other complications
- swelling of the liver, bleeding from the liver
- cancer of the kidney
- psoriasis-like skin condition, cancer of the skin, paleness of the skin
- increase of platelets or plasma cells (a type of white cell) in the blood, blood clot in small blood vessels (thrombotic microangiopathy)
- partial or total loss of vision
- decreased sex drive
- hallucinations, restlessness
- drooling
- sensitivity to light
- rapid breathing
- hernia
- brittle or weak nails
- abnormal protein deposits in your vital organs
- coma
- intestinal ulcers
- multi-organ failure.

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 BORTEZOMIB ZYDUS.

5. How to store BORTEZOMIB ZYDUS

- Store at or below 25 °C.
- Protect from light.
- Keep the vial in the outer carton until required for use.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton or container.
- 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 BORTEZOMIB ZYDUS contains

The active substance in BORTEZOMIB ZYDUS 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 BORTEZOMIB ZYDUS looks like and contents of the pack

A white to off-white colour, lyophilised powder or cake.

BORTEZOMIB ZYDUS is packed in 10 mL, 13 mm USP Type I clear tubular glass vials with 13 mm RTU, double slotted, grey colour, bromobutyl rubber stopper and 13 mm aluminium seal

with black flip-off top. One vial is packed in an outer carton.

Holder of certificate of registration

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This leaflet was last revised in

Date of registration: 10 September 2024

Date of revision: Not applicable.

Registration number

54/26/0835.084