PATIENT INFORMATION LEAFLET FOR BORTIV

SCHEDULING STATUS

S4

BORTIV 1 mg/0,4 ml; 2,5 mg/1 ml & 3,5 mg/1,4 ml

(Solution for Injection)

Each ml contains 2,5 mg of Bortezomib

Contains sugar: 25 mg/ml of Mannitol

Read all of this leaflet carefully before you are given BORTIV

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

1. What BORTIV is and what it is used for

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

BORTIV is used for the treatment of multiple myeloma (a cancer of the bone marrow)

- In combination with the 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 are given BORTIV.

BORTIV should not be administered to you

- If you are hypersensitive (allergic) to bortezomib, or any of the other ingredients of **BORTIV**
- If you have severe lung or heart problems.
- If you have severe liver problems.

Warnings and precautions

Tell your doctor or health care provider before being given the injection if you have:

- Diabetes (a blood sugar condition).
- Liver disease.
- Kidney disease or if you are on dialysis.
- Diarrhoea, constipation, nausea or vomiting, as this may become worse during **BORTIV** treatment.
- A bleeding or blood clotting disorder.
- A low level of platelet or white or red blood cells, as these conditions may become worse during treatment with **BORTIV**.
- A history of fainting, dizziness or light-headedness.
- Shortness of breath or cough.
- Seizures.
- Symptoms of tumour lysis syndrome such as muscle cramping, muscle weakness, confusion, visual loss or disturbances and shortness of breath.
- Memory loss, trouble thinking, difficulty with walking or loss of vision.
- Herpes or a history of shingles.
- High or low blood pressure.

- Nerve problems such as numbness, burning pain or tingling feeling. This effect may become worse during **BORTIV** treatment.
- 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 are pregnant or breastfeeding.

Take special care with BORTIV:

If you have mantle cell lymphoma ((a blood cancer in the lymph glands) and are given the medicine rituximab with **BORTIV** you should tell your doctor:

- If you think you have a 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.
- When thalidomide is used, particular attention to pregnancy testing and prevention requirements is needed (see **Pregnancy, breastfeeding and fertility**).

Children and adolescents

BORTIV has not been studied in children or adolescents and therefore should not be used in this patient population.

Elderly

There is no evidence to suggest that dose adjustments are necessary in the elderly.

Other medicines and BORTIV

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

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

- Ketoconazole, used to treat fungal infections.
- Ritonavir, used to treat 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, used to treat diabetes.

BORTIV with food and drink

Since, **BORTIV** is given through intravenous bolus administration, it will not be affected by food or drink.

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 taking this medicine.

Pregnancy

- Females of childbearing capacity should use effective contraceptive measures during treatment and for 3 months following **BORTIV**.

Breastfeeding

- It is not known whether **BORTIV** is excreted in human milk, therefore mothers are advised against breastfeeding while receiving **BORTIV** because of the potential for serious undesirable effects.
- If a patient wishes to restart breastfeeding after treatment, she should be advised to discuss the appropriate timing with her healthcare professional.

When **BORTIV** is given in combination with thalidomide, you must

follow the pregnancy prevention programme for thalidomide. Thalidomide causes birth defects and foetal death.

Driving and using machines

BORTIV may impair your ability to drive and use machines. **BORTIV** might cause tiredness, fainting or blurred vision. Do not drive, operate machinery, or do anything else that could be dangerous until you know how **BORTIV** affects you.

BORTIV contains mannitol

At doses that exceeds 10 g of mannitol, **BORTIV** may have a laxative effect.

3. How to receive BORTIV

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

BORTIV IS FOR INTRAVENOUS USE.

BORTIV will be administered by a healthcare professional experienced in the use of cytotoxic medicines.

BORTIV reconstitution solution before administration. This will be done by a healthcare professional.

Injection into a vein is rapid (bolus), taking 3 to 5 seconds.

Your doctor will work out your dose of **BORTIV** according to your height and weight (body surface area).

The usual starting dose of **BORTIV** is 1,3 mg/m^2 body surface
area twice weekly for two weeks (days 1, 4, 8 and 11) followed by a 10-day
rest period (days 12-21). This 3 week period is considered a treatment cycle. At least 72 hours should be between consecutive doses of **BORTIV**.

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 and on your underlying conditions (e.g. liver problems).

Progressive multiple myeloma:

When **BORTIV** is given alone, you will receive 4 doses of **BORTIV** intravenously on days 1, 4, 8 and 11, followed by a 10-day 'rest period' without treatment. This 21-day period (3 weeks) corresponds to one treatment cycle. You might receive up to 8 cycles (24 weeks).

Previously untreated multiple myeloma:

If you have not been treated before for multiple myeloma, and you are not suitable for blood stem cell transplantation you will receive **BORTIV** together with two other medicines; melphalan and prednisone. In this case, the duration of a treatment cycle is 42 days (6 weeks). You will receive 9 cycles (54 weeks).

- In cycles 1 to 4, **BORTIV** is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
- In cycles 5 to 9, **BORTIV** is administered once weekly on days 1, 8, 22 and 29.

Melphalan (9 mg/m^2) and prednisone (60 mg/m^2) are both given orally on days 1, 2, 3 and 4 of the first week of each cycle.

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

If you are given more BORTIV than you should

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

If you forget to take BORTIV

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

Call your doctor for instructions if you will miss an appointment for your bortezomib injection

4. Possible side effects

BORTIV can have side effects.

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

If any of the following happens, stop taking BORTIV 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'

These are all very serious side effects. If you have them, you may have had a serious reaction to **BORTIV**. 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:

Frequent:

- Treatment with **BORTIV** can very commonly 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 **BORTIV**, 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.
- Low blood pressure, which may lead to fainting, high blood pressure.
- Reduced functioning of your kidneys, failing of your kidneys.

- Infections, including pneumonia, respiratory infections, bronchitis, fungal infections, coughing with phlegm, urinary tract infections, herpes virus infections, ear infection and cellucitis.
- Shingles (localised including around the eyes or spread across the body), itching of the skin, lumps on the skin or dry skin, redness of the skin, different types of rash.
- Chest discomfort, chest pains or shortness of breath with exercise, increased or reduces heart rate.
- Facial blushing or tiny broken capillaries.
- Heartburn.
- Stomach pain, bleeding from your bowels or stomach, bleeding from mucosal membranes e.g., mouth, vagina.
- Alteration of liver functioning.
- Muscle cramps, muscle spasms, muscle weakness, pain in your limbs, muscle pain, bone pain.
- Blurred vision, infection of the outermost layer of the eye and the inner surface of the eyelids (conjunctivitis).
- Nose bleeds.
- Swelling of body, to include around eyes and other parts of the body.

Less frequent:

- Heart failure, heart attack, angina, inflammation of the lining around your heart or fluid around your heart.
- Inflammation of a vein, blood clots in your veins and lungs, problems with blood clotting.
- Insufficient circulation.
- Cerebrovascular disorders (limited or no blood flow to affected areas of the brain).
- Paralysis, seizures, falling, movement disorders.
- 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, breathing that becomes shallow, difficult or stops, wheezing.

- Hiccups, speech disorder.
- Increased or decreased urine production (due to kidney damage), painful passing of urine or blood/proteins in the urine, fluid retention.
- Hypersensitivity (allergic reaction).
- Hearing loss, deafness or ringing in the ears, ear discomfort, bleeding from the ears.
- Hormone abnormalities which may affect salt and water absorption.
- Overactive or underactivity of thyroid gland.
- Inability to produce enough insulin or resistance levels of insulin.
- Irritated or inflamed eyes, excessively teary eyes, painful eyes, dry eyes, eye infections, 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.
- Redness or pain at the injection site, injection device related disorders.
- Mouth pain, tooth infection.
- Inflammation of the pancreas (pancreatitis), obstruction of the bile duct.
- Genital pain, problem having an erection, genital swelling.
- Swelling / inflammation of the liver (hepatitis), bleeding from the liver.
- Flushing.
- Discolouration of the veins.
- Bleeding in the brain.
- Breast disorders.
- Vaginal tears.
- Cysts in the lining of joints.
- Breakdown of muscle fibres leading to other complications.
- Cancer of the kidney.
- Paleness of the skin.

- Abnormal reaction to blood transfusions.
- Gallstones.
- Hernia.
- Injuries.
- Abnormal protein deposits in your vital organs.
- Coma.
- Intestinal ulcers.
- Multi-organ failure.
- Death.

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

Tell your doctor as soon as possible if you notice any of the following:

Frequent:

- 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 (getting sick), loss of appetite, tiredness (fatigue), feeling weak.
- 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.
- Headache
- General ill feeling, pain, vertigo, light-headedness, a feeling of weakness or loss of consciousness.
- Shivering.
- Flu-like illness.
- Dehydration.
- Weight loss, weight increase, loss of taste, increase in appetite.

- Difficulty or problems with sleeping, excessive sweating, anxiety, mood swings, depressed mood, restlessness or agitation, changes in your mental status, disorientation.
- A sore mouth or lip, dry mouth, mouth ulcers or throat pain.

Less frequent:

- Abnormal or change in, or reduced sensation feeling, hearing, tasting, smelling), attention disturbances, twitching.
- Altered levels of consciousness, confusion, memory impairment or loss.
- Hair loss and abnormal hair texture.
- Thirst.
- Inability to tolerate alcohol consumption.
- Brittle or weak nails.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website or to the Holder of certificate of registration through the mail: pvg.cdma@heterogroups.com.

5. How to store BORTIV

- Store all medicines out of reach of children.
- Store at 2°C - 8°C, in a dry place, well closed in the original container, protected from light and moisture.
- Keep the vial in the outer carton until required for use.
- There are no special storage instructions for **BORTIV**.

- Do not store in a bathroom.
- Do not use after the expiry date stated on the label / carton / bottle.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicines in drains or sewerage system.

6. Contents of the pack and other information

What BORTIV contains

The active substance is bortezomib.

The other ingredients are mannitol (25 mg/ml), Sodium chloride, Sodium Hydroxide, Hydrochloric acid Concentrated, Water for injection.

What BORTIV looks like and contents of the pack

BORTIV 1 mg/0.4 ml

Type 1 glass 10 ml-vial with a Igloo GCB Grey EPP rubber stopper and Orange colour flip off seal contacting 2,5 mg / ml of Bortezomib

BORTIV 2.5 mg/1 ml

Type 1 glass 10 ml-vial with a Igloo GCB Grey EPP rubber stopper and White colour flip off seal contacting 2,5 mg / ml of Bortezomib

BORTIV 3.5 mg/1.4 ml

Type 1 glass 10 ml-vial with a Igloo GCB Grey EPP rubber stopper and Yellow matte top colour flip off seal contacting 2,5 mg / ml of Bortezomib

Each vial placed into a carton box. Each pack contains 1 single-use vial together with a package insert.

Holder of Certificate of Registration

Hetero Drugs South Africa (Pty) Ltd

Waterfall corporate campus,

Building no. 2, first floor,

74 waterfall drive,

Midrand 2066.

Tel.: 0126441220

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BORTIV 1 mg/0.4 ml: 57/26/0412.409

BORTIV 2.5 mg/ml: 57/260413.410

BORTIV 3.5 mg/1.4 ml: 57/26/0414.411

Access to the corresponding Professional Information

Hetero Drugs South Africa (Pty) Ltd

Waterfall corporate campus,

Building no. 2, first floor,

74 waterfall drive,

Midrand 2066.

Tel.: 0126441220

Applicant/PHRC: ***Hetero Drugs South Africa (Pty) Ltd***

Product proprietary name: ***BORTIV 1 mg/0.4 ml, 2.5 mg/ml & 3.5 mg/1.4 ml***

Dosage form and strength: ***Solution for Injection.***
Each ml contains 2,5 mg of Bortezomib.