PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

Schedule 4

VELCADE® 1,0 mg

VELCADE® 3,5 mg

powder for solution for injection for intravenous use

Bortezomib

Read all of this leaflet carefully before you are given VELCADE

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

What is in this leaflet

1. What VELCADE is and what it is used for

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

VELCADE 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 VELCADE

VELCADE should not be administered to you:

- If you are allergic (hypersensitive) to the active substance or to any of the other ingredients of VELCADE.

Warnings and precautions

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

Special care should be taken with VELCADE:

- If you have a low level of red blood cells, platelets, or white blood cells, as these conditions may become worse during treatment with VELCADE.
- If you have had any bleeding problems.
- If you are suffering from diarrhoea, constipation or nausea and vomiting, as this may become worse during VELCADE 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.
- If you have had any problems in the past with numbness, tingling, or pain in the hands or feet (neuropathy). This effect may become worse during VELCADE treatment.
- If you have any problems with your heart or with your blood pressure.

- 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 experienced or have new or increased shortness of breath or cough.
- Weakness, vomiting, cramps, fits, excess fluid buildup, heart failure, irregular heart rhythm and fainting may occur as symptoms of tumour lysis syndrome.

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

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

Other medicines and VELCADE

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.) The use of VELCADE 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 anti-diabetics.

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 healthcare provider for advice before receiving this medicine.

VELCADE must not be used if you are pregnant or breastfeeding.

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

If you wish to restart breastfeeding after VELCADE treatment, you must discuss this with your doctor, pharmacist or other healthcare professional, who will tell you when it is safe to do so.

Driving and using machines

VELCADE 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 to use VELCADE

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

You will be given VELCADE 1 mg intravenously (into the vein).

VELCADE 1 mg is for intravenous use.

You will receive VELCADE in a specialised medical unit, under the supervision of a doctor

experienced in the use of cytotoxic medicines.

VELCADE powder has to be dissolved before administration. This will be done by a healthcare professional. The resulting solution is then injected into a vein**.**
Injection into the vein is rapid, taking 3 to 5 seconds.

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

Monotherapy

When VELCADE is given alone, one cycle of treatment with VELCADE 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 VELCADE 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, VELCADE is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
In cycles 5 to 9, VELCADE 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.

Your doctor will tell you how long your treatment with VELCADE will last. Do not stop any treatment unless your doctor tells you to do so. If you have the impression that the effect of VELCADE is too strong or too weak, tell your doctor or pharmacist.

If you are given more VELCADE than you should

Since a healthcare professional will administer VELCADE, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to take VELCADE

Since a healthcare provider will administer VELCADE, it is unlikely that the dose will be missed.

4. Possible side effects

VELCADE can cause side effects. Not all side effects reported for VELCADE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking VELCADE, please consult your doctor, pharmacist or other health care professional for advice.

Swelling around the eyes or face (which may rarely be due to a serious allergic reaction), or swelling in the ankles, wrists, arms or legs.
These are all very serious side effects. If you have them, you may have had a serious allergic reaction to VELCADE. You may need urgent medical attention or hospitalisation.

Treatment with VELCADE 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 VELCADE, 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.

Side effects may occur at certain frequencies, which are classified as follows:

Frequent:

- 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, shivering fits.
- Shortness of breath without exercise.
- Feeling sick (nausea) or vomiting, 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.
- Muscle pain, tiredness, headache.
- Herpes zoster infection (including disseminated).
- Rash
- Sudden fall of blood pressure on standing which may lead to fainting.
- Depression which may be severe, confusion.
- General ill feeling, dizziness, light-headedness, or a feeling of weakness.
- Changes in potassium in your blood, too much sugar in your blood.
- Chest pains or coughing with phlegm, shortness of breath with exercise.
- Different types of rash and/or itching, lumps on the skin or dry skin.
- Redness of the skin or redness and pain at the injection site.
- Dehydration.
- Heartburn, bloating, belching, wind or stomach pain.

- A sore mouth or lip, dry mouth, mouth ulcers or throat pain.
- Weight loss, loss of taste.
- Muscle cramps, bone pain, pain in your limbs or back.
- Blurred vision.
- Nose bleeds.
- Difficulty in sleeping, sweating, anxiety.
- Overtiredness (fatigue).
- Pneumonia, bronchitis, infection of the sinus passages.

Less frequent:

- Palpitations (sensation of rapid or irregular heart beat), changes in heartbeat, heart failure, heart attack, chest pain, chest discomfort or decreased ability of the heart to work.
- Bleeding from your bowels or stomach, bloody stools, bleeding in the brain, bleeding from the liver or bleeding from mucosal membranes e.g. mouth.
- Poor movement in the intestines (including blockages).
- Paralysis, seizures.
- Breathing becomes shallow, difficult or stops, wheezing, and difficulty in breathing, cough that produces frothy sputum that may be tinged with blood or coughing blood.
- Increased or decreased urine production (due to kidney damage), painful passing of urine or blood/proteins in the urine.
- Yellow discolouration of eyes and skin (jaundice).
- Loss of attention, restlessness or agitation, changes in your mental status, mood swings.
- Facial blushing or tiny broken capillaries.
- Hearing loss, deafness or ringing in the ears.
- Changes in calcium, sodium, magnesium, and phosphates in your blood, too little sugar in your blood.
- Hormone abnormality affecting salt and water absorption.
- Irritated eyes, excessively wet or dry eyes, discharge from the eyes, abnormal vision, eye

infections (including herpes zoster), bleeding of the eye or sensitivity to light.

- Damage to the optic nerve and blindness.
- Swelling of your lymph nodes.
- Joint or muscle stiffness, muscle spasms or twitching, pain in your bottom.
- Hair loss.
- Allergic reactions.
- Mouth pain, retching.
- Abdominal pain.
- Weight increase.
- Severe skin reactions, which may have blisters and involve the mouth, throat, eyes and genitals that can be life-threatening (Stevens Johnson Syndrome and toxic epidermal necrolysis).
- Posterior Reversible Encephalopathy Syndrome (PRES), a severe reversible brain condition which includes seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems.
- Inflammation of the blood vessels that can appear as small red or purple dots (usually on the legs) to bruise-like patches on the skin.
- Progressive multifocal leukoencephalopathy, a rare usually fatal viral disease characterised by progressive damage or inflammation of the white matter of the brain at multiple locations.

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via “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 VELCADE.

Alternatively, you may report side effects experienced with VELCADE directly to Janssen Pharmaceutica (see section ‘Holder of the Certificate of Registration’ for contact details or visit www.janssen.com).

5 How to store VELCADE

VELCADE will be stored in the pharmacy.

Store all medicines out of reach of children.

Store at or below 30 °C. Keep the container in the outer carton in order to protect from light.

Do not use after the expiry date stated on the vial and the carton.

The reconstituted solution may be stored for 8 hours at 25 °C when stored in the original vial and/or a syringe prior to administration with a maximum of 8 hours in the syringe.

6 Contents of the pack and other information

VELCADE contains a medicine called bortezomib. . Each vial contains 1 mg or 3,5 mg (as a mannitol boronic ester). VELCADE will be dissolved in a sterile, sodium chloride (salt) solution. After reconstitution, 1 mL of solution for intravenous injection contains 1 mg bortezomib.

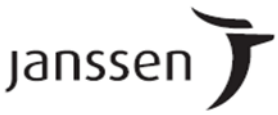
The other ingredient of VELCADE is mannitol (E 421).

What VELCADE looks like and contents of the pack

A white to off-white cake or powder.

VELCADE is supplied as a single-use 5 mL and 10 mL clear, colourless glass vial with a grey bromobutyl stopper and an aluminium seal with green flip-off cap (5 mL vial) and royal blue flip-off cap (10 mL vial).
The 5 mL vial contains 11 mg powder for solution for injection and the 10 mL vial contains 38,5 mg powder for solution for injection.
Each vial is contained in a transparent blister pack (consisting of a tray with a lid) which is placed into an outer carton together with a professional information insert/patient information leaflet.

Holder of certificate of registration



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Access to the corresponding Professional Information

Included in the carton, accompanying this patient information leaflet.