PATIENT INFORMATION LEAFLET (SUBCUTANEOUS ADMINISTRATION)

SCHEDULING STATUS:

S4

VELBOR IV lyophilised powder for solution for injection.

Bortezomib

Contains sugar (35 mg mannitol).

Read all of this leaflet carefully before you are given VELBOR IV

- 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 VELBOR IV is and what it is used for
2. What you need to know before you use VELBOR IV
3. How to use VELBOR IV
4. Possible side effects
5. How to store VELBOR IV
6. Contents of the pack and other information

1. What VELBOR IV is and what it is used for

VELBOR IV contains bortezomib, one of a group of medicines called proteasome inhibitors. Proteasomes play an important role in controlling cell function and growth. By interfering with their function, bortezomib can kill cancer cells.

VELBOR IV is used for the treatment of multiple myeloma (a cancer of the bone marrow) in adults:

- in combination with the 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 administered VELBOR IV

VELBOR IV should not be administered:

- if you are hypersensitive (allergic) to bortezomib, boron or any of the other ingredients of VELBOR IV (see section 5)
- if you have certain severe heart or lung problems (acute diffuse infiltrative pulmonary and pericardial disease).

Warnings and precautions

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

- if you have experienced or have new or increased shortness of breath or cough
- if you have a low level of red blood cells, platelets, or white blood cells, as these conditions may become worse during treatment with VELBOR IV
- if you have had any bleeding problems as you may required blood transfusions during treatment
- if you experience any stomach problems such as diarrhoea, constipation, nausea or vomiting. These side effects usually occur early in treatment and may persist for several cycles of therapy. Your doctor may prescribe you an additional medicine to help control these symptoms, and you may be advised to increase your intake of fluids or electrolytes, to prevent or treat dehydration
- 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 VELBOR IV treatment
- if you have a history of seizures or epilepsy as you will need to be closely monitored

- if you have a history of fainting, dizziness or light-headedness as VELBOR IV may worsen this condition
- if you have any problems with your heart or with your blood pressure
- if you have any problems with your kidneys as your condition will need to be closely monitored
- if you have any problems with your liver as your dose may need to be reduced
- if you have or have had hepatitis B virus (HBV) as your doctor will closely monitor you for signs of active hepatitis B (see below)
- if you suffer from weakness, vomiting, cramps, fits, excess fluid build-up, heart failure, irregular heart rhythm and fainting during treatment, these may occur as symptoms of tumour lysis syndrome and your doctor will need to closely monitor you
- 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 develop symptoms including memory loss, trouble thinking, difficulty with walking or loss of vision. These may be signs of a serious brain infection and your doctor may suggest further testing and follow-up
- if you develop shingles (localised including around the eyes or spread across the body). Your doctor may prescribe you an antiviral medicine if you have previously experienced shingles (a viral infection which causes a painful rash) since shingles may reactivate during treatment with VELBOR IV
- if you have porphyria (a rare blood disorder) as your doctor may want to change your medicine or closely monitor you
- if you have recently been vaccinated, as this may possibly cause a bad reaction with VELBOR IV.

If you are given the medicine rituximab with VELBOR IV you should tell your doctor if you are a carrier of hepatitis B or have previously had a hepatitis B infection. Patients who have had

hepatitis B may have a repeated attack, which can be fatal. If you have a history of hepatitis B infection, your doctor will closely monitor you for signs of active hepatitis B.

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

Children and adolescents:

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

Other medicines and VELBOR IV

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

In particular, tell your doctor if you are taking any of the following medicines:

- Ketoconazole (to treat fungal infections) as the effects of VELBOR IV may be intensified
- Ritonavir (to treat HIV infection) as the effects of VELBOR IV may be intensified
- Rifampicin (antibiotic to treat bacterial infections) as rifampicin reduces the effects of VELBOR IV
- Carbamazepine, phenytoin or phenobarbital (to treat epilepsy) as these medicines reduce the effect of VELBOR IV
- St. John's Wort *(Hypericum perforatum)* (to treat depression or other conditions) reduce the effect of VELBOR IV
- Oral antidiabetics as your doctor may monitor your blood glucose levels or adjust the dose of your antidiabetic medication.

VELBOR IV with food and drink

VELBOR IV can be administered with or without food.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare provider for advice before being administered VELBOR IV.

Both men and women receiving Bortezomib must use effective contraception during and for up to 3 months after treatment. If, despite these measures, pregnancy occurs, tell your doctor immediately.

The use of VELBOR IV should be avoided during pregnancy and breastfeeding.

Driving and using machines:

VELBOR IV can make you feel tired, dizzy, or faint, or cause blurred vision. Driving and operating machinery should be avoided until you know how VELBOR IV affects you.

It is not always possible to predict to what extent VELBOR IV may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which VELBOR IV affects them.

3. How to receive VELBOR IV

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

You will not be expected to give yourself VELBOR IV**.** It will be injected under the skin by a person who is qualified to do so.

VELBOR IV lyophilised powder for solution for injection will be reconstituted and diluted to the correct concentration by a healthcare provider.

The resulting solution will be either injected under the skin (in the thigh or abdomen).

Your doctor will calculate your dose of VELBOR IV according to your height and weight (body surface area). The usual starting dose is 1,3 mg/m^2 body surface area twice a week.

Monotherapy:

You will receive 4 doses of VELBOR IV on days 1, 4, 8 and 11, followed by a 10-day 'rest period' with no treatment. This 21-day period (3 weeks) corresponds to one treatment cycle. You may receive up to 8 cycles (24 weeks).

Combination therapy:

If you have not been treated before for multiple myeloma, you will receive VELBOR IV 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, VELBOR IV is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
- In cycles 5 to 9, VELBOR IV 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 VELBOR IV will last. Do not stop treatment early because your condition may not be resolved.
If you have the impression that the effect of VELBOR IV is too strong or too weak, tell your doctor or pharmacist.

If you are administered more VELBOR IV than you should:

Since a healthcare provider will administer VELBOR IV, they will control the dosage. However, in the event of overdosage, your doctor will manage the overdosage.

If you missed a dose of VELBOR IV:

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

4. Possible side effects

VELBOR IV can have side effects.

Not all side effects reported for VELBOR IV are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using VELBOR IV, please consult your doctor, pharmacist or other healthcare provider for advice.

If any of the following happens, stop using VELBOR IV 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 allergic reaction to VELBOR IV. 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:

- seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems, paralysis
- chest pain or discomfort, shortness of breath, changes in the way your heart beats, for example, if you notice it is beating faster, dizziness, nausea and cold to the touch
- bleeding from the gums, nose, mouth, stomach, reddish or pink urine, unexpected bruising
- stomach pain or swelling, problems passing urine, muscle weakness or paralysis (Tumour lysis syndrome)
- Stevens-Johnson syndrome or other serious skin disorder (begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters
- chest pain, angina
- difficulty breathing

- signs of recurrent infections such as fever or sore throat
- passing less urine than is normal for you, swelling of the legs, ankles or feet (symptoms of kidney failure).

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

Treatment with VELBOR IV 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 VELBOR IV, 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 gums, 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:
Frequent side effects:

- shingles, skin rash (itching skin, lumps on the skin or dry skin), pneumonia, bronchitis, sinusitis, viral or fungal infection, the common cold, cold sores
- loss or increase of appetite, dehydration, low levels of potassium in the blood, increased blood sugar (hyperglycaemia)
- confusion, depression, sleep disorders (insomnia), anxiety sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage, pins-and-needles sensation, headache, dizziness, taste disturbance, reduced sense of touch or sensation, tremor
- blurred vision, eye pain, loss of balance (vertigo)
- low blood pressure or sudden fall in blood pressure

- lightheaded, especially when standing up, inflammation of a vein or blood clots, red or purple spots on the skin due to broken blood vessels
- nosebleed, cough, runny nose, chest infection
- vomiting or retching, diarrhoea, nausea, constipation, stomach pain, bloating or cramps, swollen mouth or lips, heartburn or indigestion, loose stools, passing wind, hiccups, mouth ulcers, pain or difficulty swallowing, dry mouth, fever
- abnormal liver blood test results
- rash, hives, red or itchy skin, inflamed, scaly or dry skin, puffy eyes, swelling of the eyelids or face, increased sweating or night sweats
- muscle pain, weakness, stiffness or cramps, joint or bone pain, joint swelling or stiffness, back pain, swelling of the feet and legs
- kidney problems, painful urination
- extreme tiredness, fever, lack of energy or strength, shaking or shivering, generally feeling unwell, flu-like illness, swelling of the legs or ankles, chest pain, general pain or swelling
- weight loss.

Less frequent side effects:

- heart failure, heart attack, chest pain, chest discomfort, increased or reduced heart rate, palpitations, inflammation of the lining around the heart or fluid around the heart
- Posterior Reversible Encephalopathy Syndrome (PRES), a severe reversible brain condition (which includes seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems), discoloration or swelling of the veins, bleeding in the brain, hot flushes, blood clots, problems with blood clotting, insufficient blood circulation
- confusion, depression, problems sleeping, anxiety, agitation, delirium, hallucinations, restlessness, mood swings or mental health changes, irritability, abnormal dreams, suicidal thoughts

- disorders that affect your lungs, preventing your body from getting enough oxygen – difficulty or changes in breathing, shortness of breath, shortness of breath without exercise, breathing that becomes shallow, difficult or stops, wheezing, dry throat, hoarseness, lung infection or collapse, asthma, nasal congestion, nose bleeds, cough, itchy, blocked or runny nose, chest or sinus pain, tightness of throat, phlegmy cough
- bleeding from your bowels or stomach, bloody stools, change in bowel habits, vomiting blood, belching, bleeding or painful gums, excessive saliva, coated or discoloured tongue, retching, gastritis, irritable bowel syndrome, incontinence, abdominal pain, lip pain
- hepatitis, yellow discolouration of eyes and skin (jaundice), Budd–Chiari syndrome (the clinical symptoms caused by blockage of the hepatic veins), swelling of the liver, bleeding from the liver
- inflammation of the joints in the fingers, toes, buttock and jaw, joint or muscle stiffness, sense of heaviness, joint effusion, cysts in the lining of joints (synovial cysts), fracture, inflammation of the spinal nerve, breakdown of muscle fibres leading to other complications, muscle spasm, muscle twitching, falls
- migraine, paralysis or weakness in lower half of body, seizures, fainting, problems concentrating, jerky movements, sciatica (leg pain which usually starts in the lower back), speech problems, restless leg syndrome, hiccups, speech disorders, drooling
- altered levels of consciousness, memory impairment or loss
- falling, movement disorders, abnormal/change in, or reduced sensation (feeling, hearing, tasting, smelling), attention disturbance, trembling, twitching
- inflammation of a vein, blood clots in your veins and lungs
- 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, bleeding from the gums, nose or mouth, any bleeding that will not stop, reddish or pink urine, unexpected bruising (you may have less platelets in your blood than is normal)
- overactive or underactive thyroid gland

- changes to the normal contents of your blood, including the amount of glucose, vitamins or minerals in your blood, diabetes, gout, increased appetite, alcohol intolerance, fluid retention
- inflammation of the pancreas, obstruction of the bile duct
- kidney failure, kidney damage, painful passing of urine or blood/proteins in the urine, fluid retention, cancer of the kidney, sudden urge to urinate, inability to completely empty the bladder, needing to urinate more than usual or problems urinating, loss of bladder control, pain in the side of the abdomen (due to kidney stones), pain in the upper abdomen or back, blood in the urine
- blood cell changes which could make you feel unwell (your doctor will detect these by taking a blood test), swelling of the lymph glands, increased platelets in the blood, blood clots, blood thickening, swelling of the face
- abnormal protein deposits in your vital organs (amyloidosis)
- infections including sepsis, pneumonia, bronchitis, sinusitis, bacteria, viral or fungal infections, respiratory infections, catheter related infection, coughing with phlegm, flu-like illness, glandular fever, chickenpox, stomach or urinary tract infections, oral thrush, inflammation of the eyelids, viral or bacterial meningitis (symptoms may include fever, light sensitivity, headache, and a stiff neck), gastroenteritis, skin, ear or tooth infection, genital herpes, tonsillitis, Epstein-Bar virus infection, cellulitis
- irritated or inflamed eyes, excessively wet eyes, painful eyes, dry eyes, eye infections (conjunctivitis), discharge from the eyes, abnormal vision, bleeding of the eye, extreme light sensitivity, blindness
- hearing loss, deafness or ringing in the ears, ear discomfort, partial loss of hearing
- mouth pain, infections or inflammation of the mouth, mouth ulcers, oesophagus, stomach and intestines, sometimes associated with pain or bleeding, poor movement of the intestines (including blockage), abdominal or oesophageal discomfort, difficulty swallowing
- genital pain, problem having an erection, breast disorders female, vaginal tears and bleeding, genital swelling, decreased sex drive, pelvic pain, genital ulcer

- inflammation or bleeding of mucosal membranes (e.g. mouth and vagina), stabbing or burning pain (due to nerve damage), injection site complications such as bleeding, swelling, redness, burns, tenderness or pain, feeling cold
- skin infections, skin ulcers, skin rash, acne, cold and night sweats, blisters, hair loss and abnormal hair texture, psoriasis like skin condition, cancer of the skin, paleness of the skin, heat rash, sensitivity of the skin to sunlight
- injection site or injection device related disorders, falls and injuries, abnormal protein deposits in your vital organs, intestinal ulcers, multi-organ failure, hernia, delayed wound healing, body temperature change, coma, sudden death, change in thirst, tightness, discomfort or sensation of pressure on the chest, general pain or swelling
- changes in calcium, sodium, magnesium, and phosphates in your blood, too little sugar in your blood
- hormone abnormality which may affect salt and water absorption, inability to produce enough insulin or resistance to normal levels of insulin, redness or pain at the injection site.

The following side effects have been reported but the frequency for them to occur is not known:

- reversible posterior leukoencephalopathy syndrome, a brain disorder that predominantly affects the white matter of the brain characterised by headache, nausea and vomiting, seizures, visual disturbances, altered senses
- decreased brain function due to toxins or infection, nerve damage
- deafness
- lung disorder
- inflammation or injury of the large bowel
- pressure sores.

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 "**6.04 Adverse Drug 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 VELBOR IV.

5. How to store VELBOR IV

Store all medicines out of reach of children.

Powder: Store at or below 25 ˚C.

Keep the vial in the carton until required for use.

The reconstituted solution may be stored for up to 8 hours at 25 °C in the original vial and/or a syringe prior to administration. Discard any unused portion.

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

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What VELBOR IV contains

The active substance is bortezomib. Each vial contains 3,5 mg bortezomib (mannitol boronic ester).

After reconstitution each 1 mL of solution contains 2,5 mg bortezomib.

VELBOR IV contains 35 mg mannitol.

The other ingredients are:

Mannitol

What VELBOR IV looks like and contents of the pack

VELBOR IV lyophilised powder for solution for injection is a white to off-white lyophilised mass. After reconstitution with 0,9 % sodium chloride solution for injection: A clear, colourless solution. VELBOR IV is packed into Clear 10 mL glass vial with grey rubber plug, aluminium seal with red flip off cap. Each vial is placed in an outer carton. Each vial contains 3,5 mg bortezomib.

Holder of Certificate of Registration

MC Pharma (Pty) Ltd

62 Constantia Avenue

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0157

South Africa

This leaflet was last revised in

To be allocated

Registration number

A50/26/0960

PATIENT INFORMATION LEAFLET (INTRAVENOUS ADMINISTRATION)

SCHEDULING STATUS:

S4

VELBOR IV lyophilised powder for solution for injection.

Bortezomib

Contains sugar (35 mg mannitol)

Read all of this leaflet carefully before you are given VELBOR IV

- 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

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2. What you need to know before you use VELBOR IV
3. How to use VELBOR IV
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6. Contents of the pack and other information

1. What VELBOR IV is and what it is used for

VELBOR IV contains bortezomib, one of a group of medicines called proteasome inhibitors. Proteasomes play an important role in controlling cell function and growth. By interfering with their function, bortezomib can kill cancer cells.

VELBOR IV is used for the treatment of multiple myeloma (a cancer of the bone marrow) in adults:

- in combination with the 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 administered VELBOR IV

VELBOR IV should not be administered:

- if you are hypersensitive (allergic) to bortezomib, boron or any of the other ingredients of VELBOR IV (see section 5)
- if you have certain severe heart or lung problems (acute diffuse infiltrative pulmonary and pericardial disease).

Warnings and precautions

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

- if you have experienced or have new or increased shortness of breath or cough
- if you have a low level of red blood cells, platelets, or white blood cells, as these conditions may become worse during treatment with VELBOR IV
- if you have had any bleeding problems as you may required blood transfusions during treatment
- if you experience any stomach problems such as diarrhoea, constipation, nausea or vomiting. These side effects usually occur early in treatment and may persist for several cycles of therapy. Your doctor may prescribe you an additional medicine to help control these symptoms, and you may be advised to increase your intake of fluids or electrolytes, to prevent or treat dehydration
- 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 VELBOR IV treatment
- if you have a history of seizures or epilepsy as you will need to be closely monitored

- if you have a history of fainting, dizziness or light-headedness as VELBOR IV may worsen this condition
- if you have any problems with your heart or with your blood pressure
- if you have any problems with your kidneys as your condition will need to be closely monitored
- if you have any problems with your liver as your dose may need to be reduced
- if you have or have had hepatitis B virus (HBV) as your doctor will closely monitor you for signs of active hepatitis B (see below)
- if you suffer from weakness, vomiting, cramps, fits, excess fluid build-up, heart failure, irregular heart rhythm and fainting during treatment, these may occur as symptoms of tumour lysis syndrome and your doctor will need to closely monitor you
- 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 develop symptoms including memory loss, trouble thinking, difficulty with walking or loss of vision. These may be signs of a serious brain infection and your doctor may suggest further testing and follow-up
- if you develop shingles (localised including around the eyes or spread across the body). Your doctor may prescribe you an antiviral medicine if you have previously experienced shingles (a viral infection which causes a painful rash) since shingles may reactivate during treatment with VELBOR IV
- if you have porphyria (a rare blood disorder) as your doctor may want to change your medicine or closely monitor you
- if you have recently been vaccinated, as this may possibly cause a bad reaction with VELBOR IV.

If you are given the medicine rituximab with VELBOR IV you should tell your doctor if you are a carrier of hepatitis B or have previously had a hepatitis B infection. Patients who have had

hepatitis B may have a repeated attack, which can be fatal. If you have a history of hepatitis B infection, your doctor will closely monitor you for signs of active hepatitis B.

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

Children and adolescents:

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

Other medicines and VELBOR IV

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

In particular, tell your doctor if you are taking any of the following medicines:

- Ketoconazole (to treat fungal infections) as the effects of VELBOR IV may be intensified
- Ritonavir (to treat HIV infection) as the effects of VELBOR IV may be intensified
- Rifampicin (antibiotic to treat bacterial infections) as rifampicin reduces the effects of VELBOR IV
- Carbamazepine, phenytoin or phenobarbital (to treat epilepsy) as these medicines reduce the effect of VELBOR IV
- St. John's Wort *(Hypericum perforatum)* (to treat depression or other conditions) reduce the effect of VELBOR IV
- Oral antidiabetics as your doctor may monitor your blood glucose levels or adjust the dose of your antidiabetic medication.

VELBOR IV with food and drink

VELBOR IV can be administered with or without food.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare provider for advice before being administered VELBOR IV.

Both men and women receiving Bortezomib must use effective contraception during and for up to 3 months after treatment. If, despite these measures, pregnancy occurs, tell your doctor immediately.

The use of VELBOR IV should be avoided during pregnancy and breastfeeding.

Driving and using machines:

VELBOR IV can make you feel tired, dizzy, or faint, or cause blurred vision. Driving and operating machinery should be avoided until you know how VELBOR IV affects you.

It is not always possible to predict to what extent VELBOR IV may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which VELBOR IV affects them.

3. How to receive VELBOR IV

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

You will not be expected to give yourself VELBOR IV**.** It will be given to you intravenously (injected into a vein) by a person who is qualified to do so.

VELBOR IV lyophilised powder for solution for injection will be reconstituted and diluted to the correct concentration by a healthcare provider.

The resulting solution will be injected into a vein. Injection into the vein is very rapid, taking 3 to 5 seconds.

Your doctor will calculate your dose of VELBOR IV according to your height and weight (body surface area). The usual starting dose is 1,3 mg/m^2 body surface area twice a week.

Monotherapy:

You will receive 4 doses of VELBOR IV on days 1, 4, 8 and 11, followed by a 10-day 'rest period' with no treatment. This 21-day period (3 weeks) corresponds to one treatment cycle. You may receive up to 8 cycles (24 weeks).

Combination therapy:

If you have not been treated before for multiple myeloma, you will receive VELBOR IV 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, VELBOR IV is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
- In cycles 5 to 9, VELBOR IV 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 VELBOR IV will last. Do not stop treatment early because your condition may not be resolved.
If you have the impression that the effect of VELBOR IV is too strong or too weak, tell your doctor or pharmacist.

If you are administered more VELBOR IV than you should:

Since a healthcare provider will administer VELBOR IV, they will control the dosage. However, in the event of overdosage, your doctor will manage the overdosage.

If you missed a dose of VELBOR IV:

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

4. Possible side effects

VELBOR IV can have side effects.

Not all side effects reported for VELBOR IV are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using VELBOR IV, please consult your doctor, pharmacist or other healthcare provider for advice.

If any of the following happens, stop using VELBOR IV 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 allergic reaction to VELBOR IV. 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:

- seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems, paralysis
- chest pain or discomfort, shortness of breath, changes in the way your heart beats, for example, if you notice it is beating faster, dizziness, nausea and cold to the touch
- bleeding from the gums, nose, mouth, stomach, reddish or pink urine, unexpected bruising
- stomach pain or swelling, problems passing urine, muscle weakness or paralysis (Tumour lysis syndrome)
- Stevens-Johnson syndrome or other serious skin disorder (begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters

- chest pain, angina
- difficulty breathing
- signs of recurrent infections such as fever or sore throat
- passing less urine than is normal for you, swelling of the legs, ankles or feet (symptoms of kidney failure).

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

Treatment with VELBOR IV 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 VELBOR IV, 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 gums, 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:

Frequent side effects:

- shingles, skin rash (itching skin, lumps on the skin or dry skin), pneumonia, bronchitis, sinusitis, viral or fungal infection, the common cold, cold sores
- loss or increase of appetite, dehydration, low levels of potassium in the blood, increased blood sugar (hyperglycaemia)
- confusion, depression, sleep disorders (insomnia), anxiety sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage, pins-and-needles sensation, headache, dizziness, taste disturbance, reduced sense of touch or sensation, tremor
- blurred vision, eye pain, loss of balance (vertigo)

- low blood pressure or sudden fall in blood pressure
- lightheaded, especially when standing up, inflammation of a vein or blood clots, red or purple spots on the skin due to broken blood vessels
- nosebleed, cough, runny nose, chest infection
- vomiting or retching, diarrhoea, nausea, constipation, stomach pain, bloating or cramps, swollen mouth or lips, heartburn or indigestion, loose stools, passing wind, hiccups, mouth ulcers, pain or difficulty swallowing, dry mouth, fever
- abnormal liver blood test results
- rash, hives, red or itchy skin, inflamed, scaly or dry skin, puffy eyes, swelling of the eyelids or face, increased sweating or night sweats
- muscle pain, weakness, stiffness or cramps, joint or bone pain, joint swelling or stiffness, back pain, swelling of the feet and legs
- kidney problems, painful urination
- extreme tiredness, fever, lack of energy or strength, shaking or shivering, generally feeling unwell, flu-like illness, swelling of the legs or ankles, chest pain, general pain or swelling
- weight loss.

Less frequent side effects:

- heart failure, heart attack, chest pain, chest discomfort, increased or reduced heart rate, palpitations, inflammation of the lining around the heart or fluid around the heart
- Posterior Reversible Encephalopathy Syndrome (PRES), a severe reversible brain condition (which includes seizures, high blood pressure, headaches, tiredness, confusion, blindness or other vision problems), discoloration or swelling of the veins, bleeding in the brain, hot flushes, blood clots, problems with blood clotting, insufficient blood circulation
- confusion, depression, problems sleeping, anxiety, agitation, delirium, hallucinations, restlessness, mood swings or mental health changes, irritability, abnormal dreams, suicidal thoughts

- disorders that affect your lungs, preventing your body from getting enough oxygen – difficulty or changes in breathing, shortness of breath, shortness of breath without exercise, breathing that becomes shallow, difficult or stops, wheezing, dry throat, hoarseness, lung infection or collapse, asthma, nasal congestion, nose bleeds, cough, itchy, blocked or runny nose, chest or sinus pain, tightness of throat, phlegmy cough
- bleeding from your bowels or stomach, bloody stools, change in bowel habits, vomiting blood, belching, bleeding or painful gums, excessive saliva, coated or discoloured tongue, retching, gastritis, irritable bowel syndrome, incontinence, abdominal pain, lip pain
- hepatitis, yellow discolouration of eyes and skin (jaundice), Budd–Chiari syndrome (the clinical symptoms caused by blockage of the hepatic veins), swelling of the liver, bleeding from the liver
- inflammation of the joints in the fingers, toes, buttock and jaw, joint or muscle stiffness, sense of heaviness, joint effusion, cysts in the lining of joints (synovial cysts), fracture, inflammation of the spinal nerve, breakdown of muscle fibres leading to other complications, muscle spasm, muscle twitching, falls
- migraine, paralysis or weakness in lower half of body, seizures, fainting, problems concentrating, jerky movements, sciatica (leg pain which usually starts in the lower back), speech problems, restless leg syndrome, hiccups, speech disorders, drooling
- altered levels of consciousness, memory impairment or loss
- falling, movement disorders, abnormal/change in, or reduced sensation (feeling, hearing, tasting, smelling), attention disturbance, trembling, twitching
- inflammation of a vein, blood clots in your veins and lungs
- 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, bleeding from the gums, nose or mouth, any bleeding that will not stop, reddish or pink urine, unexpected bruising (you may have less platelets in your blood than is normal)
- overactive or underactive thyroid gland

- changes to the normal contents of your blood, including the amount of glucose, vitamins or minerals in your blood, diabetes, gout, increased appetite, alcohol intolerance, fluid retention
- inflammation of the pancreas, obstruction of the bile duct
- kidney failure, kidney damage, painful passing of urine or blood/proteins in the urine, fluid retention, cancer of the kidney, sudden urge to urinate, inability to completely empty the bladder, needing to urinate more than usual or problems urinating, loss of bladder control, pain in the side of the abdomen (due to kidney stones), pain in the upper abdomen or back, blood in the urine
- blood cell changes which could make you feel unwell (your doctor will detect these by taking a blood test), swelling of the lymph glands, increased platelets in the blood, blood clots, blood thickening, swelling of the face
- abnormal protein deposits in your vital organs (amyloidosis)
- infections including sepsis, pneumonia, bronchitis, sinusitis, bacteria, viral or fungal infections, respiratory infections, catheter related infection, coughing with phlegm, flu-like illness, glandular fever, chickenpox, stomach or urinary tract infections, oral thrush, inflammation of the eyelids, viral or bacterial meningitis (symptoms may include fever, light sensitivity, headache, and a stiff neck), gastroenteritis, skin, ear or tooth infection, genital herpes, tonsillitis, Epstein-Bar virus infection, cellulitis
- irritated or inflamed eyes, excessively wet eyes, painful eyes, dry eyes, eye infections (conjunctivitis), discharge from the eyes, abnormal vision, bleeding of the eye, extreme light sensitivity, blindness
- hearing loss, deafness or ringing in the ears, ear discomfort, partial loss of hearing
- mouth pain, infections or inflammation of the mouth, mouth ulcers, oesophagus, stomach and intestines, sometimes associated with pain or bleeding, poor movement of the intestines (including blockage), abdominal or oesophageal discomfort, difficulty swallowing
- genital pain, problem having an erection, breast disorders female, vaginal tears and bleeding, genital swelling, decreased sex drive, pelvic pain, genital ulcer

- inflammation or bleeding of mucosal membranes (e.g. mouth and vagina), stabbing or burning pain (due to nerve damage), injection site complications such as bleeding, swelling, redness, burns, tenderness or pain, feeling cold
- skin infections, skin ulcers, skin rash, acne, cold and night sweats, blisters, hair loss and abnormal hair texture, psoriasis like skin condition, cancer of the skin, paleness of the skin, heat rash, sensitivity of the skin to sunlight
- injection site or injection device related disorders, falls and injuries, abnormal protein deposits in your vital organs, intestinal ulcers, multi-organ failure, hernia, delayed wound healing, body temperature change, coma, sudden death, change in thirst, tightness, discomfort or sensation of pressure on the chest, general pain or swelling
- changes in calcium, sodium, magnesium, and phosphates in your blood, too little sugar in your blood
- hormone abnormality which may affect salt and water absorption, inability to produce enough insulin or resistance to normal levels of insulin, redness or pain at the injection site.

The following side effects have been reported but the frequency for them to occur is not known:

- reversible posterior leukoencephalopathy syndrome, a brain disorder that predominantly affects the white matter of the brain characterised by headache, nausea and vomiting, seizures, visual disturbances, altered senses
- decreased brain function due to toxins or infection, nerve damage
- deafness
- lung disorder
- inflammation or injury of the large bowel
- pressure sores.

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 "**6.04 Adverse Drug 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 VELBOR IV.

5. How to store VELBOR IV

Store all medicines out of reach of children.

Powder: Store at or below 25 ˚C.

Keep the vial in the carton until required for use.

The reconstituted solution may be stored for up to 8 hours at 25 °C in the original vial and/or a syringe prior to administration. Discard any unused portion.

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

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What VELBOR IV contains

The active substance is bortezomib. Each vial contains 3,5 mg bortezomib (mannitol boronic ester).

After reconstitution each 1 mL of solution contains 1 mg bortezomib.

VELBOR IV contains 35 mg mannitol.

The other ingredients are:

Mannitol

What VELBOR IV looks like and contents of the pack

VELBOR IV lyophilised powder for solution for injection is a white to off-white lyophilised mass. After reconstitution with 0,9 % sodium chloride solution for injection: A clear, colourless solution. VELBOR IV is packed into Clear 10 mL glass vial with grey rubber plug, aluminium seal with red flip off cap. Each vial is placed in an outer carton. Each vial contains 3,5 mg bortezomib.

Holder of Certificate of Registration

MC Pharma (Pty) Ltd

62 Constantia Avenue

Mnandi

0157

South Africa

This leaflet was last revised in

To be allocated

Registration number

A50/26/0960