1.3.2 Approved Patient Information Leaflet

SCHEDULING STATUS

S4

PATIENT INFORMATION LEAFLET

DEVACAD powder for solution for injection

Bortezomib

(Contains Sugar: 35,0 mg mannitol)

Read all of this leaflet carefully before you are given DEVACAD

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

What is in this leaflet:

1. What DEVACAD is and what it is used for

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

DEVACAD 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 take DEVACAD

DEVACAD should not be administered to you:

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

Warnings and precautions

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

Special care should be taken with DEVACAD:

- If you have a low level of red blood cells, platelets, or white blood cells, as these conditions may become worse during treatment with DEVACAD.
- If you have had any bleeding problems.

- If you are suffering from diarrhoea, constipation or nausea and vomiting, as this may become worse during DEVACAD treatment.
- If you have a history of fainting, dizziness or light-headedness.
- 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 DEVACAD 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 build up, heart failure, irregular heart rhythm and fainting which may occur as symptoms of tumour lysis syndrome.
- If you have experienced or have new or increased memory loss, confusion, trouble thinking, difficulty with walking or loss of vision.
- Seizures
- Shingles (localised including around the eyes or spread across the body).

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before being given this medicine.

Children and adolescents

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

Other medicine and DEVACAD:

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

The use of DEVACAD 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.
- ritonavir, an antiretroviral medication used to treat HIV/AIDS
- 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, 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 healthcare provider for advice before receiving this DEVACAD.

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

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

If you wish to restart breastfeeding after DEVACAD 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

DEVACAD 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.

It is not always possible to predict to what extent DEVACAD 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 DEVACAD affects them

DEVACAD contains mannitol which may have a mild laxative effect.

3. How to use DEVACAD

You will be given DEVACAD intravenously (into the vein) or subcutaneously (under the skin).

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

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

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

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

Monotherapy

When DEVACAD is given alone, one cycle of treatment with DEVACAD 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 DEVACAD 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, DEVACAD is administered twice weekly on days 1, 4, 8, 11, 22, 25, 29 and 32.
- In cycles 5 to 9, DEVACAD 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 DEVACAD will last. If you have the impression that the effect of DEVACAD is too strong or too weak, tell your doctor or pharmacist.

If you take more DEVACAD than you should

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

If you forget to take DEVACAD

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

4. Possible side effects

DEVACAD can have side effects.

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

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

- severe itching of the skin or raised lumps on the skin, swelling around the eyes, face, lips, tongue and /or throat, which may cause difficulty in swallowing,
- muscle cramping, muscle weakness,
- confusion, visual loss or disturbances, blindness, fits (seizures), headaches,
- shortness of breath, swelling of your feet, ankles, wrists, arms or legs or changes in your heartbeat, high blood pressure, tiredness, feeling dizzy/faint, collapse,
- coughing and breathing difficulties, tightness in the chest or chest pain.
- Swelling around the eyes or face or tongue, (which may rarely be a serious allergic reaction)
- Swelling in the ankles, wrists, arms and legs

These are all very serious side effects. If you have them, you may have had a serious reaction to DEVACAD. You may need urgent medical attention or hospitalisation.

Treatment with DEVACAD 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 DEVACAD, to check your blood cell counts.

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.

Tell your doctor if you notice any of the following:

Frequent 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
- 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
- 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
- General ill feeling, pain, vertigo, light-headedness, a feeling of weakness or loss of consciousness
- Shivering
- Infections, including pneumonia, respiratory infections, bronchitis, fungal infections, coughing with phlegm, flu like illness
- Shingles (localised including around the eyes or spread across the body)
- Chest pains or shortness of breath with exercise
- Different types of rashes
- 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
- Changes in liver functioning
- A sore mouth or lip, dry mouth, mouth ulcers or throat pain
- Weight loss, loss of taste
- Muscle cramps, muscle spasms, muscle weakness, pain in your limbs
- Blurred vision
- Infection of the outermost layer of the eye and the inner surface of the eyelids (conjunctivitis)
- Nose bleeds

- Difficulty or problems in sleeping, sweating, anxiety, mood swings, depressed mood, restlessness or agitation, changes in your mental status, disorientation
- Swelling of body, to include around eyes and other parts of the body of rashes

Less frequent side effects:

- Palpitations (sensation of rapid or irregular heartbeat), 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 of 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, vomiting.
- 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.
- Dry mouth/throat.
- Problems with blood clotting, poor circulation, swelling of a vein,
- Infections including urinary tract infections, the flu, herpes virus infections, ear infection and cellulitis.
- Overactive thyroid gland

- Genital pain, decreased sex drive
- Tooth infection
- Swelling of the pancreas, blockage of the bile duct
- 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.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects via https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of DEVACAD

5. How to store DEVACAD

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

DEVACAD will be stored in the pharmacy

Store at or below 25 °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

What DEVACAD contains

The active substance is bortezomib.

Each vial contains 3,5 mg (as a mannitol boronic ester).

DEVACAD will be dissolved in a sterile, sodium chloride (salt) solution.

After reconstitution for intravenous injection, 1 mL of solution for contains 1 mg bortezomib.

After reconstitution for subcutaneous injection, 1 mL of solution for contains 2,5 mg bortezomib.

The other ingredients of DEVACAD are mannitol, tert-butanol and Water for injection.

What DEVACAD looks like and contents of the pack

A white to off-white cake or powder.

DEVACAD is supplied as a single-use 10 mL Type-I clear glass tubular vial stoppered with grey rubber stopper and sealed with an aluminium seal having a Taxim Blue PP disc. The vial is packed in a pre-printed carton with a professional information insert/patient information leaflet.

NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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