1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

PROTECADE 1 mg powder for solution for injection

PROTECADE 3,5 mg powder for solution for injection

Bortezomib

Contains sugar: Mannitol

Read all of this leaflet carefully before you are given PROTECADE

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

What is in this leaflet

1. What PROTECADE is and what it is used for

PROTECADE contains the active substance bortezomib, a proteasome inhibitor.

Proteasomes play an important role in controlling cell function and growth. By interfering with their function, bortezomib can kill cancer cells.

PROTECADE is used for the treatment of:

- Multiple myeloma (a cancer of the bone marrow) in combination with the medicines melphalan and prednisone.
- For patients whose disease is worsening (progressive) after receiving at least one prior treatment
- Mantle cell lymphoma (a type of cancer affecting the lymph nodes) for patients who have received at least one prior line of therapy, one which should have included anti-cancer chemotherapy medicine (anthracycline or mitoxantrone and/or rituximab) as part of their chemotherapy

2. What you need to know before you receive PROTECADE

PROTECADE should not be administered to you

- if you are hypersensitive (allergic) to bortezomib, boron, or any of the other ingredients of PROTECADE (listed in section 6).
- if you have certain severe lung or heart problems.

Warnings and precautions

Special care should be taken with PROTECADE

Tell your doctor or health care provider before being given the injection if you suffer from

- shingles (localised including around the eye or spread across the body). Your doctor may give you preventative medicines to prevent an occurrence or re-occurrence of shingles.

- low number of red or white blood cells, bleeding problems and/or low number of platelets in your blood. Your doctor will carefully monitor your blood counts. You may require blood/platelet transfusions.
- diarrhoea, constipation, nausea or vomiting. You doctor will prescribe medicines to help you with these side effects.
- damaged nerves outside the brain and spinal cord. Symptoms include numbness, pain or a burning feeling in the feet or hands.
- seizures
- heart or blood pressure problems
- kidney problems
- moderate to severe liver problems or Hepatitis B infection
- symptoms of tumour lysis syndrome such as muscle cramping, muscle weakness, confusion, visual loss or disturbances and shortness of breath
- swelling of joints,
- headache, confusion, memory loss, trouble thinking, difficulty with walking or loss of vision
- fainting, dizziness or light-headedness in the past
- shortness of breath or cough

You will have to take regular blood tests before and during your treatment with PROTECADE to check your blood cell counts regularly.

If you have mantle cell lymphoma, you may experience peripheral neuropathy (disease of the nerves), rash and pruritis (itching of the skin).

If you have multiple myeloma, you may experience thrombocytopenia (low platelets), neutropenia (low white blood cells), anaemia, nausea, vomiting and pyrexia (raised body temperature).

You must read the package leaflets of all medicinal products to be taken in combination with PROTECADE for information related to these medicines before starting treatment with PROTECADE. When thalidomide is used, particular attention to pregnancy testing and prevention requirements is
needed (see Pregnancy and breast-feeding in this section).

Children and adolescents

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

Other medicines and PROTECADE

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

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
- Omeprazole, used to treat ulcers

- 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 antidiabetics

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

Safety in pregnancy and lactation has not been established.

You should not use PROTECADE if you are pregnant, unless clearly necessary.

Thalidomide causes birth defects and foetal death. When PROTECADE is given in combination with thalidomide you must follow the pregnancy prevention programme for thalidomide.

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

Breastfeeding

It is not known if PROTECADE is excreted in human milk. Due to the potential for serious undesirable effects, you should not breastfeed while using PROTECADE.

Fertility

No data on male and female fertility is available.

Driving and using machines

It is not always possible to predict to what extent PROTECADE may interfere with your daily activities. You should ensure that you do not engage in activities requiring mental alertness, judgment and/or sound coordination and vision e.g. driving, riding, flying, sailing or operating machines/equipment until you are aware of the measure to which PROTECADE affects you.

PROTECADE may cause tiredness, dizziness, fainting or blurred vision.

Do not drive or operate tools or machines if you experience such side effects.

3. How to use PROTECADE

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

PROTECADE may be administered as an intravenous injection (into the vein), or subcutaneously (under your skin). Injection into a vein is rapid, taking 3 to 5 seconds. Injection under the skin is in either the thighs or the abdomen.

The dose will be decided by your doctor according to your height and weight (body surface area) and will be administered twice a week. Your doctor will tell you how long your treatment with PROTECADE will last. If you have the impression that the effect of PROTECADE is too strong or too weak, tell your doctor or pharmacist.
PROTECADE has to be dissolved before administration. This will be done by a healthcare provider.

If you receive more PROTECADE than you should

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

If you forget to receive PROTECADE

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

4. Possible side effects

PROTECADE can have side effects.

Not all side effects reported for PROTECADE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving PROTECADE, please consult your health care provider for advice.
If any of the following happens, stop receiving PROTECADE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Shortness of breath, swelling of your feet or changes in your heart beat, high blood pressure, tiredness, feeling dizzy/fainting
- Coughing and breathing difficulties or tightness in the chest, chest pain
- Serious allergic reaction (anaphylactic shock) signs of which may include severe itching of the skin or raised lumps on the skin, swelling of the face, lips, tongue and /or throat, which may cause difficulty in swallowing, collapse.

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

Treatment with PROTECADE can commonly cause a decrease in the numbers of red and white blood cells and platelets in your blood. You will have to take regular blood tests before and during your treatment to check your blood counts regularly. You may experience a reduction in the number of:

- Platelets, which maybe make you more prone to bruising, or to bleeding without obvious injury
- 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 immediately if you notice any of the following:

- Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage
- Fever
- Nausea, vomiting, loss of appetite, diarrhoea
- Constipation with or without bloating
- Tiredness
- Muscle cramping, muscle weakness
- Confusion, visual loss or disturbances, blindness, seizures, headaches.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- Infection of the lungs (pneumonia), respiratory infection, infection caused by fungus
- Reduction in the number of red blood cells and or white blood cells
- Loss of appetite, dehydration
- Low levels of potassium, sodium and calcium in the blood
- Anxiety, mood and sleep disorders
- Sensitivity, numbness, tingling or burning sensation of the skin, or pain in the hands or feet, due to nerve damage
- Dizziness, tiredness, headache, a feeling of weakness, loss of consciousness

- Swelling or redness of the lining of the white part of the eye caused by an infection (conjunctivitis), blurred vision
- Low and high blood pressure
- Shortness of breath, nose bleeds, cough
- Nausea, vomiting, diarrhoea, constipation
- Rash, itching of the skin, dry skin
- Muscle spasms, muscle pain, muscle weakness, bone pain, pain in the limbs
- Reduced kidney function
- Painful or difficulty in urinating
- Fever, chills
- Weight loss

Less frequent side effects:

- Infection caused by bacteria or virus, infection of the skin, ear, tooth
- Abnormal tissue growth
- Blood clotting problems
- Increase of platelets or plasma cells (a type of white cell) in the blood
- Blood clot in small blood vessels (thrombotic microangiopathy)
- Skin reactions and disorders
- Swelling of joints
- Over and under active thyroid gland

- High levels of potassium, sodium and calcium in the blood, Vitamin B deficiency
- Gout
- Increased appetite, unable to tolerate alcohol
- Paralysis, seizures, falling, movement disorders, abnormal or change in, or reduced sensation (feeling, hearing, tasting, smelling), attention disturbance, trembling, twitching
- 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
- Hearing loss, deafness or ringing in the ears, ear discomfort
- Heart failure, heart attack, angina, chest pain, chest discomfort, increased or reduced heart rate
- Inflammation of the lining around your heart or fluid around your heart
- Insufficient circulation, causing sudden exhaustion or weakness
- 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
- 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

- 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, vomiting of blood
- Budd–Chiari syndrome (the clinical symptoms caused by blockage of the hepatic veins)
- Liver disorders such as inflammation, bleeding, failure
- Arthritis including inflammation of the joints in the fingers, toes and the jaw
- Muscle twitching, muscle stiffness
- Kidney failure, kidney damage causing increased or decreased urine production, painful passing of urine or blood/proteins in the urine
- Genital pain, erection problems
- Breast disorders, vaginal bleeding
- Injection site reactions, such as bleeding, pain, allergic reaction

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 nurse. You can also report side effects to SAHPRA via the "**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 PROTECADE.

5. How to store PROTECADE

Store all medicines out of reach of children.

Store at or below 25 ºC. Keep the vial in the outer carton, protected from light.

Reconstituted solution:

The reconstituted solution may be stored up to 8 hours at 25 °C in the dark, both in a vial and in a polypropylene syringe.

For single use only, discard any unused portion.

6. Contents of the pack and other information

What PROTECADE contains

The active substance is bortezomib.

The other ingredient is Mannitol (E421)

What PROTECADE looks like and contents of the pack

PROTECADE is a white to off-white, cake or powder.

PROTECADE 1 mg powder for solution for injection is packed into glass type I vials (6 ml) with a bromobutyl rubber stopper and a green flip-off cap.

PROTECADE 3.5 mg powder for solution for injection is packed into glass type I vials (10 ml) with a bromobutyl rubber stopper and a blue flip-off cap.

Holder of Certificate of Registration

Adcock Ingram Critical Care (Pty) Ltd

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Tel: 011 494 8000

Registration number

53/26/0177 PROTECADE 1 mg

53/26/0178 PROTECADE 3.5 mg